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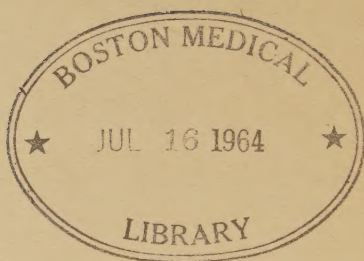


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CANCER:

Its Cause,
Treatment and Prevention

A. T. BRAND



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CANCER:

ITS CAUSE, TREATMENT AND PREVENTION.

BY

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FOREWORD.

THE contents of this book consist of a series of addresses delivered at intervals to the East Yorks and North Lincoln Branch of the British Medical Association at Hull, and published in the *British Medical Journal*, *Lancet*, and other medical periodicals.

Although the time covered is from 1902 to 1910, so little advance has been made in the elucidation of the disease that they might have been written quite recently.

With regard to these addresses the late C. B. Keetley, Esq., F.R.C.S., in his book, *The Prevention of Cancer*, published in 1907, wrote a special appendix to the following effect :—

“ I should like to refer readers, on the question of the ætiology of cancer, to the extremely able papers and addresses of Dr. Alex. Theodore Brand, of Driffeld. An abstract of the first appeared in the *British Medical Journal* for July 26th, 1902, and the address has been published in full by the *Aberdeen University Press*. This address,” which was his Presidential one, “ contains the most able statement of the case for the ‘ Infection Theory ’ of cancer, which I have read.”

His other papers are :—

“ The Exogenesis of Cancer,” *Quarterly Medical Journal*, May, 1903.

“ The Causation of Cancer,” *The Practitioner*, October, 1903.

Several of these addresses were copiously quoted from by the late Roswell Park, Professor of Surgery, Buffalo, U.S.A., in his address, "The Nature of the Cancerous Process," read before the International Society of Surgery, at Brussels, in 1908.

Additions have been made occasionally referring to more recent events.

A. T. B.

DRIFFIELD.

INTRODUCTION.

THAT Cancer is as typically an auto-infective disease as are syphilis and tuberculosis, is unquestionable.

That it is due to the action of an extrinsic cause, as are these other diseases, is to many equally obvious, while its communicability from individual to individual, in some lower animals, has been exhaustively proved by experiment.

This communicability has been most grudgingly admitted, inasmuch as the successful results of contagion have been termed merely "grafts."

But, if the disease is successfully transferred from one individual to another, and, after pursuing its typical course, causes the death of the host, that is exactly what occurs when anyone contracts an admittedly infectious disease having a fatal termination.

The chief stumbling block to the acceptance of the exogenesis of cancer is the failure of all attempts, up to the present, to discover the causal agent or parasite.

This is unreasonable, since many diseases are freely admitted to be due to parasites where the causal parasite has not been identified.

It is difficult to understand the mentality of those who repudiate the possibility of the exogenesis of cancer, especially when one considers the causation of disease generally, and the great part that parasites play in its production.

It may be too sweeping to assert that all disease is due to parasitism, but, on the other hand, it is not sufficiently

realized to what an extraordinary extent parasitism is responsible.

If all reference to diseases caused by parasitism was excluded from medical treatises what remains would be extremely meagre, while treatises on tropical diseases would be non-existent.

There are indeed some who deny the existence of microbes, and others who deny, even if they do exist, any causal relationship to disease, but as regards the great majority of medical men who have the solution of the cancer problem at heart, I hope that what I have written will induce them to admit, at least, the "sweet reasonableness" of an extrinsic cause of cancer.

A general acceptance of this belief would lead to a more hopeful and determined effort to deal with the disease by anti-parasitic treatment, as is done so successfully in other diseases of extrinsic origin, and insure its prophylaxis.

It is greatly to be deprecated that the Ministry of Health should so entirely ignore cancer, a disease which carries off a large proportion of the population annually, since every tenth person over the age of 35 falls a victim to the disease.

I cannot but feel that cancer is quite as important a disease as tuberculosis, even more so, since the ætiology of the latter has been established, while that of cancer has not.

Notification and investigation of all cases of cancer are urgently called for, and it ought not to be left to the generosity of the public to try to effect its elucidation. The State is responsible for the health of the people, and shirking this responsibility is inexcusable.

CANCER :

Its Cause, Treatment, and Prevention.

THE ÆTIOLOGY OF CANCER.¹

BEFORE inflicting upon you what can only by a euphemism be termed a "Presidential Address," I desire to thank you very sincerely for the great honour you have conferred upon me, by electing me to the Presidency of this Branch for the coming year.

The choice of a subject on which to address so erudite and critical an audience has proved exceedingly difficult, but I have chosen as my theme a consideration of that dread disease, which is equally familiar to us all, whatever position we may occupy in the medical world, which may be very aptly described by the term that Robert Burns applied to toothache, *viz.*, the "Hell of all diseases," whose true nature we are as yet ignorant of, which is, without doubt, increasingly prevalent, and which is inevitably fatal.

It is almost unnecessary to say that I refer to cancer,

¹ An abstract of this address is published in the *British Medical Journal* of July 26th, 1902, and in full by the Aberdeen University Press.

a subject of absorbing interest, and to this I wish to direct your attention. I regret that the time at my disposal is so short that it is impossible to treat this subject with the fulness its importance merits, therefore what I shall be able to bring before you this afternoon can be only sketchy and imperfect. At the outset I may state that under the generic term of "cancer" I include all that is clinically described as "malignant."

This mysterious disease, which is alike the scourge of mankind and the reproach of medicine, has, for decades of centuries, eluded and defied all efforts made for the elucidation of its nature and cause.

There is ever a fascination about a mystery, and the discovery of the cause of cancer has long been to the young and enthusiastic medico what the invention of a practicable perpetual motion machine is, or used to be, to the budding engineer, or what the discovery of the *elixir vitæ*, or the philosopher's stone was to the alchemist of the past; and it is devoutly to be hoped that the medico will meet with better success in his quest than the others have done.

Since, unfortunately, no one, so far, has been successful in the search for the cause of cancer, and as no one has discovered a reliable empiric remedy for it, there has been engendered in the medical profession a mental attitude of the most profound pessimism, amounting indeed to absolute fatalism, and this, if possible, obtains even more strongly with the laity.

Defeat must not, however, be permitted to paralyse our energies, it should rather be a stimulus to renewed efforts.

We must recognize no such word as "impossible" and, without doubt, one day, success will be assured.

If success has not been attained it has not been for want of endeavouring to solve this problem.

Numberless specific causes have been suggested, and many theories have been evolved, but the very number and variety of these simply go to prove that the true cause has still to be discovered.

ALLEGED SPECIFIC CAUSES.

Among many other alleged specific causes cancer has been ascribed to over-indulgence in tea, in sugar, to the consumption of the succulent but harmless tomato, to excessive flesh-eating, and to excessive consumption of common salt.

Well, cancer was in existence long before tea and sugar became articles of diet, and thousands die of cancer who never heard of the existence of a tomato.

With regard to excessive flesh-eating, this would, doubtless, give rise to an excess of uric acid in the blood, which is alleged to cause many of the ills to which poor mortals are heirs, and among others to cancer; but when we find cancer occurring freely in the Hindoos, who eat flesh sparingly if at all, and also when it occurs in such strict vegetarians as the horse and cow, we fail to see an exclusive causal relation to cancer on the part of flesh-eating, excessive or otherwise.

Of these alleged causes common salt alone is a vital necessity to the organism, and all warm-blooded animals partake of it to the necessary degree, without exception.

Braithwaite alleges that pigs alone of domesticated animals do not have salt given to them, and that, in consequence, they are not subject to cancer.

Pigs do appear to enjoy immunity from cancer to a

notable extent, but, whatever the reason may be, it is certainly not abstention from salt. The pig consumes quite as much salt as the dog, in which cancer is, *e.g.*, quite common. The source of the salt is, obviously, the food given, which is specially rich in salt, *e.g.*, skimmed milk and the *olla podrida* of the swill-tub.

Probably the reason is that pigs are not permitted to live long enough to contract a disease chiefly found in advanced age.

It is altogether unreasonable to suggest that a specific disease, such as cancer is, can possibly be caused by excessive consumption of flesh, as alleged by Mitchell Banks, or by excessive consumption of salt, as alleged by Braithwaite. It is not unreasonable, however, to assume that the tissues may be so irritated by this consumption as to be rendered more vulnerable, so that a condition precedent is established, but this must be the limit of their evil influence.

The confounding of *post* and *propter* constitutes a common fallacy, and it is equally illogical to suggest, as the cause of cancer, that which is not universally applicable.

THEORIES.

Of the many theories advanced I shall very briefly pass in review a few of the best known and most important.

The first I shall mention is Cohnheim's, which attributes malignant tumours to awakened growth of embryonic rudiments.

Such rudiments are rare, but even then I presume something must awaken them; and it is reasonable to suppose that this something may be the x cause of cancer.

Another theory is that of Thiersch, who maintained that epithelioma is due to a war between columns of epithelial cells growing downwards and loops of blood-vessels growing upwards, until they meet and interlock in deadly combat. This may, and no doubt does, more or less accurately describe what goes on in an epithelial growth, but it does not suggest the *casus belli*, which is the cause of malignancy we are in search of.

Then Hanseemann thought that karyokinesis was concerned in the causation of cancer. Here again we have only a description of what goes on in the nuclei of the developing cells of malignant tumours.

Karyokinesis takes place in the nuclei of normal cells as well as in pathological ones, and if the method of mitosis differs according to the kind of cell, it is only what might be expected, but it does not suggest a cause to account for this difference, and therefore does not explain the originating cause of cancer.

Also the heterotype karyokinesis found in proliferating malignant cells is also found in normal generative tissue.

Again, there is a theory which attributes cancer to the spermatic influence of cells, whatever this may mean.

Here the cells of a tumour, having increased in number, are said to exert such an influence upon the surrounding healthy cells of the connective tissue, that the latter are stimulated likewise to increase in number, not, however, in their own proper structure, but transformed into the same type as the exciting tumour cells. Once more we have to ask, "What is the originating cause of the primary tumour which in turn exerts such a malign influence upon the surrounding connective tissue cell?" It is, doubtless, the x cause of cancer.

The last theory I shall mention is that suggested by Creighton, *viz.*, that cancer is due to the unconscious evil memory, or bad habit of the tissues. He says cancer is "the peculiar Nemesis of secretion or other epithelial action gone wrong, of long-standing catarrhs, repeated congestions, or habitual irritations of epithelial surfaces, or the peculiar liabilities of women in respect to the early obsolescence of their primary and secondary sexual structures and functions."

This is simply a statement of the "condition precedent." Irritation, *per se*, can never cause a specific disease such as cancer, though it can and does most materially assist the true cause.

Most of these theories seem to me to have been built up by dreamers at the ocular end of a microscope in histological laboratories, and there they may very well be permitted to remain as museum specimens, for all the practical value they are to any one.

No doubt they are interesting, but at the most they are only descriptive of pathological processes, or suggestive of probable contributory factorship. Nowhere do they suggest the originating cause of a specific disease.

One recent writer, who, in common with the authors of these theories, appears to believe in the autogenesis of cancer, *i.e.*, that the cause of cancer is to be found within the organism, gives it as his opinion that the cause of malignancy will only be explained when we know more of the cause of the development of foetal organs.

Alas! if we have to wait so long; for when we know that we shall know everything, even to the cause and origin of life itself, and that, I presume, will be when

we are all behind the veil, where cancer, and all other mundane evils, shall have ceased to interest us!

INFECTION THEORY.

What I conceive to be one great barrier to the discovery of the cause of cancer is the apparently universal feeling that this cause is desperately recondite and complex; whereas it may, and probably will, be found to be excessively simple, with nothing especially mysterious about it.

If we are to make any headway in the elucidation of cancer, we must discard all dreamy theories, and form a good working hypothesis, and it is the practical man, not the dreamer, who will succeed. The clinician and the experimental pathologist must combine and work upon such a hypothesis, and only abandon it when it has been proved conclusively to be untenable, and not merely because it is said to be impracticable.

Now, there is a hypothesis which suggests that the cause of cancer exists apart from the organism, *viz.*, the infection theory.

It has been stated of this theory that the negative evidence is abundant, and what little positive evidence exists will not bear criticism. Now, to say that a disease cannot be infectious because the infective agent cannot be found, or because it is not strictly analogous to another disease, known to be infectious, is pure *petitio principii*.

Infectious diseases present the widest diversity in their nature and behaviour, *e.g.*, in their length of incubation, their mode of attack, their eruptive characteristics, their sites of selection, their duration, the tendency of some to pass, and the inevitably fatal ending of others.

What can be more striking than the difference between the fulminating rapidity of action of malignant bubonic plague, cholera or yellow fever, and the very leisurely advance of leprosy; or the difference between the rose rash of enterica and the loathsome eruption of confluent variola?

The very microbes themselves display a variety not to be surpassed by a garden of flowers.

I have no doubt whatever that in time it will be found that very many diseases, of whose origin we at present know nothing, will be demonstrated to be due to microbes and their toxins.

For example, that most mysterious disease, so rapidly fatal, Landry's Paralysis, in the absence, in many cases, of all pathological signs in the spinal cord, together with the enlargement of the spleen, is shrewdly suspected of being caused by the toxin of some microbe as yet unknown.

Again, who, twenty years ago, would have suspected that tetanus is caused by the toxin of a bacillus?

From what I have read and observed, the belief has been forced upon me that the cause of cancer comes from without the organism, and that the infection theory is an excellent working hypothesis.

It is the only hypothesis, to my mind, that meets the case fully. It can explain everything in connection with cancer—its origin, its growth, its undoubted and ever-extending increase, and its behaviour generally.

It should, therefore, be the aim of us all to investigate the subject on this hypothesis, and satisfy ourselves of its truth or falsity.

We should, farther, hope, all the more fervently, that this hypothesis shall be established, when we realize

that, if cancer originates within the organism, whether from the misbehaviour of laggard embryonic rudiments, or any other peculiar misconduct of our tissues, we are confronted by the grim truth that no treatment can ever be hoped to be successful on any lines; for, if there is one thing more certain than another, so far as I can see, it is the utter hopelessness of any specific antidote to cancer fortuitously forthcoming.

Many alleged specific remedies have been announced from time to time, and many methods of treatment have been promulgated, but one and all have proved utterly futile.

Recently a sensational statement regarding the efficacy of violet leaves in cancer went the round of the lay newspapers; and cases of cancer have actually been treated, in an orthodox hospital, with the remedies of that gigantic fraud and archquack, Count Mattei.

Now, no one will deny that man's capacity for self-deception is enormous, or that the credulity of mankind is unbounded, but, when we are asked to believe that boiled violet leaves, externally applied, effected a cure of cancer of the larynx, or that *aqua simplex*, of doubtful purity, can heal a fungating mamma, or render patent a stenosed pylorus, even unquestioning faith must pause, appalled!

If, on the other hand, the cause of cancer comes from without, there is every hope that this disease will eventually be overcome, yielding to prophylaxis and specific treatment.

I admit that the weak point in this hypothesis is its extreme simplicity.

It cannot be expected to commend itself to those who are fascinated with such complex and involved

mysteries, more mouth-filling than anything else, as karyokinetic evolutions, spermatic influence of cells, awakened growth of embryonic rudiments, unconscious memory of the tissues, *et hoc genus omne*; but the simple theory of infection has this to recommend it, that it is eminently practicable, while the others are utterly impracticable.

Of course the acceptance of the infection theory involves the acceptance of the existence of an infective micro-organism, whether microzoön or microphyte, not yet discovered; but this need not stand in the way of its acceptance, since no one questions the fact that variola, pertussis, scarlatina, or morbilli, etc., are infectious and due to the influence of micro-organisms, although no germs have, so far, in these cases, been isolated.

Nor need we look to the microscopists alone for help, but to the practical observer and the experimental pathologist.

Is it too much to hope that, when the latter have established the infection hypothesis, the histologists may at length discover the special microbe, or microbes, of cancer? It is true that Scheuerlen and Doyen have reported the presence, in cancerous tumours, of microbes which they believe to be the active agents in their origin, but, so far, causal nexus has not yet been conclusively established.

HISTORICAL.

That cancer is infectious has long been a belief. In the middle of the seventeenth century, Zacutus Lusitanus stated his belief that cancer is contagious, and cited cases. In 1672 Nicolaus Tulpius, the famous

anatomist, whose portrait must be familiar to most of us from the picture painted by Rembrandt, was so sure of it that he stated that "an ulcerated cancer is just as contagious as an inflammation of the eyes." Juncker, in 1731, said that successful engrafting necessitated that the infective material should fall on a suitable place where there was already a breach of the surface. In 1773 the Academy of Medicine at Lyons discussed the subject.

EVIDENCE MUST BE CIRCUMSTANTIAL.

In the absence of a demonstrated microbe, to try to prove this hypothesis of infection, one must fall back upon inductive methods.

The evidence in favour of infection must, necessarily, be circumstantial; but such evidence need not be less valuable on that account.

The planet Neptune was not, primarily, discovered by the telescope. It was not until its exact situation had been indicated by the purely inductive reasoning of Adams and Le Verrier that it was, at length, actually seen by the telescope. These men based their hypothesis upon circumstantial evidence alone, and this evidence was the aberrant behaviour of another planet, Uranus, in its orbit.

EVIDENCE OF THE EXOGENESIS OF CANCER.

In stating the evidence in favour of the external origin of cancer, one might begin with the general statement that the cause must come from without, because the cause of, practically, all disease exists outside the body, for it is extremely problematical if any disease can possibly arise, of itself, within the organism.

This general statement, however, will not materially

help to establish the infection hypothesis, and so recourse must be had to more particular evidence.

To my mind, the great, central, fundamental and most convincing argument in favour of this hypothesis is the incontrovertible fact that cancer, once generated, spreads locally by infecting its immediate environment, and that it is disseminated metastatically by the blood current and lymph streams, the latter infecting glands *en route*.

Each metastatic mass and infected gland becomes a fresh focus of further infection and dissemination. This alone should, I think, effectually dispose of Cohnheim's theory of awakened growth of embryonic rudiments.

Another very suggestive fact is that, while cancer is at the outset a purely local disease, it becomes eventually constitutional, one of the indications of such being the gradual establishment of a so-called "cachexia." This term "cachexia," I should imagine, simply means that the victim of cancer has become saturated with the toxin of the microbe causing his disease.

That this toxin is slow in accumulating seems fortunate in view of the preparation of an antitoxin. There would be ample time for the free and, let us hope, successful exhibition of such a serum.

METASTASIS.

With regard to the secondary metastatic foci of cancer it is peculiarly characteristic of this disease that each new focus consists, histologically, of epithelial elements identical with the cells of the original primarily infected growth.

There is here no "mimicry" as has been alleged. There is undoubted reproduction of the original patho-

logical tissue itself, showing most clearly that actual cells from the primary growth have been transported along the blood and lymph channels to be deposited at fresh sites, and, being charged with the infective material, they form new and active colonies.

In other diseases where metastasis occurs, such as tubercle, actinomycosis, syphilis, and pyæmia, although the disease germs are transported by the blood and lymph, the cell elements themselves are not so transported; but this difference from cancer does not militate in the very slightest degree against the infection theory of cancer-causation.

It is only another example of the infinite variety to be found in germ-caused disease.

SELECTIVE SITES.

While primary cancer can be originated in, practically, any tissue, it has an almost exclusive selective affinity for epithelial surfaces generally, and for the mucous membrane in particular. Its favourite sites are at places which are directly and easily accessible to infective germs. We find 55 per cent. of these sites in the alimentary canal, which would suggest that the infective agent is ingested.

The remaining favourite sites are in the organs concerned in the reproduction of the species, and the nutrition of the young.

These sites are not only suggestive of infection from without, but also of the probability that the micro-organism is a microphyte and not a microzoön; for, wherever cancer grows luxuriantly and rapidly, we find present the chief desiderata for the growth of pathogenic bacteria, *viz.*, moisture, an eminently suitable

nutrient medium, a constant temperature most favourable to the growth of pathogenic bacteria, and exclusion of light and air.

One could hardly imagine a better culture chamber for bacterial growth than the alimentary canal or uterus.

Conversely, we find that cancer has not been observed in the invertebrata, very rarely in the cold-blooded vertebrata. It is chiefly found in man and domesticated mammalia. It is very rare in wild mammals. Bland-Sutton states that he found a mammary adenoma in a phalanger, and that this single case represents the extent of his knowledge concerning adenomata and carcinomata in wild mammals. This statement is emphasized by the fact that he was in close attendance in the prosector's room of the Zoological Society's Gardens for eight years, during which time he was particularly on the look-out for tumours of all kinds.

RÔLE OF IRRITATION.

The infectiousness of cancer, like that of leprosy and tubercle, does not, fortunately, seem to be very great, otherwise the increase would be much greater than it is, and it is evident that something else is necessary besides a culture chamber.

The nutrient material is not an inert substance like gelatin or bouillon, but is living tissue, capable of repelling the attacks of invading bacteria, so long as there is no breach in its continuity.

When, however, this occurs, either by accident or from long-continued irritation, vulnerability is induced, especially if at the same time the general health is impaired. In all probability cancer does not arise in

and the other two. The primary purpose of the
the other two is to provide a means of identifying
the other two.

[illegible][illegible]

This garden is one of the most beautiful in the
country, and is a garden with the finest of
flowers, and is one of the most beautiful of the
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There is a small, dark, rectangular object, possibly a piece of wood or metal, lying on the ground. It is surrounded by some dry leaves and twigs. The object appears to be a small, rectangular block, possibly a piece of wood or metal, lying on the ground. It is surrounded by some dry leaves and twigs. The object appears to be a small, rectangular block, possibly a piece of wood or metal, lying on the ground. It is surrounded by some dry leaves and twigs. The object appears to be a small, rectangular block, possibly a piece of wood or metal, lying on the ground. It is surrounded by some dry leaves and twigs.

nether garments of the majority of women would, naturally, favour access to the generative organs of the infective micro-organism, especially if its *habitat* is the soil.

Thus we find that cancer arises generally in sites rendered vulnerable by injury, or irritation, or degenerative change, and this vulnerability is greater, *a fortiori*, in the middle-aged and old, in whom the resisting power is still further reduced from the fact that, in them, decay is in excess of the power to repair.

CARCINODERMS.

The majority of infectious diseases have cutaneous affections accompanying them peculiar to each, which are commonly known as eruptions.

Now, if a well-marked characteristic cutaneous manifestation accompanied cancer in most, if not all, cases, we should have another point in common between cancer and diseases well known to be directly caused by an infective germ.

Have we any such carcinoderm (if I may coin a term analogous to syphiloderm)?

When a student, a quarter of a century ago, the first operation at which I assisted was the excision of a cancerous mamma, and it was performed by my old friend and teacher, Dr. Ogilvie Will, of the Aberdeen Royal Infirmary. While chloroform was being administered, my attention was particularly drawn to the skin over the woman's chest, which had, scattered over it, a number of bright scarlet, shining, punctate spots, unaltered by pressure and varying in size from a pin's head to a split pea. I pointed them out to Dr. Will, and on asking what they were, he told me that he

had observed such spots before in cases of mammary cancer.

These spots made a deep impression on my mind and I have looked for them ever since in such cases, and have rarely or never failed to find them, sometimes few and small, at other times larger and more numerous, but almost invariably present.

Since then I have always considered them as naturally accompanying cancer of the breast, and I have occasionally pointed them out to other surgeons doing the same operation, but without succeeding in arousing any special interest in them. Until recently I had not looked for them in cases of cancer other than mammary. A few days ago, however, I found them in a case of pelvic cancer, and in another case of cancer of rectum and liver.

When the probability of cancer being due to direct infection from without was gradually, but irresistibly, forced upon me, the question arose in my mind whether these spots are characteristic of cancer to such an extent as to entitle them to be considered pathognomonic, or whether they are merely fortuitous concomitants.

I have not observed a sufficient number of cases to form a decisive opinion, but I feel that my views have been greatly strengthened by what I read the other day in an article giving a *précis* of a paper published in the *Münchener medizinische Wochenschrift* of December last.

This article is contributed by Leser, who says that he finds a small angiomatous growth frequently occurring in the skin of patients suffering from cancer, and that he has not seen any literary notice of it in such a connection.

Freund and Hollander have recounted the existence of such growths in the skin, but they lay little stress on the occurrence.

In many cases of cancer, Leser found that a number of raised spots were present, chiefly on the skin of the trunk. The spots vary in size from that of the head of a pin to that of a lentil. They are bluish-red, or bright red in colour, and do not fade on pressure. They are angiomaticous in structure.

To ascertain the clinical significance of these spots, Leser and his assistant, Müller, investigated in fifty cases of cancer :—

1. Whether these spots usually accompanied cancer.
2. Whether they occur in either healthy subjects, or in patients suffering from diseases other than cancerous.
3. Whether their appearance is of diagnostic value.

Of these fifty cases in only one (cancer of the œsophagus), were these angiomatica absent. In one case the number of spots was seventy-six and the average number was fifteen.

They decided that the first query must be answered in the affirmative. To settle the second point they examined 300 cases of surgical and medical diseases, and found the angiomatica only in subjects of advanced age in a few cases, and probably in these cases cancer could not definitely be excluded.

Leser therefore concludes that they do not appear in healthy subjects, or in persons suffering from other diseases in early or middle life, and never, even in old age, in large numbers.

Further, when found in large numbers in young or middle-aged people, there is every reason to suspect cancer.

The detection of a number of small angiomas of the skin of apparently healthy subjects may point to a commencing cancer.

The abdomen seems to be the favourite site of the spots in internal cancer, and in other cases the skin superficial to, or in the vicinity of, the seat of the disease appears to be chiefly affected.

These spots do not appear to have any direct relationship to the cancerous growth itself, nor are they influenced by changes in the vessels of the growth.

Leser points out how important it would be, should this prove to be a reliable sign in making an early diagnosis of cancer, and distinguishing between benign and malignant tumours in cases of doubt.

The only literary notice I have been able to find of angiomas in connection with cancer was furnished me by the kind courtesy of Mr. Malcolm Morris. He referred me to a tract published in 1872 by the late Mr. Campbell de Morgan, of Middlesex Hospital, entitled, "*The Origin of Cancer.*"

In this tract (page 16), de Morgan says:—"There is another circumstance in connection with the recurrence of cancer after operation which, to my mind, is very significant. I have noticed, and it has been verified by the observations of many others, that concurrently with, or following on the development of, cancer, small outgrowths of warty, or vascular, or dermoid structure are frequent. Now, one would imagine that, if there were a cancer poison in the blood, these, or one of them, would become the seat of the disease; but it is never the case."

Again (on page 23), referring to a case under his care, he says: "From the large size of the breast the dis-

charge, which was very profuse and sanious, lodged on its upper surface and trickled down the axillary fold. In these situations there sprang up a number of small pinkish excrescences which looked something like crops of minute vascular warts. They were attached to the superficial layers of the skin only. They were found, too, only in situations where the discharge could lie, and, while in these they became more and more numerous so as to coalesce in the end and form elevated patches, not one appeared above the level of the ulcer. Even after many months these little growths had hardly extended to the deep layers of the skin. I have no doubt that the lodgment of the cancerous discharge on her irritable skin had allowed of the implantation and superficial growth of cancer germs." These angiomas were called by the Middlesex Hospital staff "de Morgan's spots," or "*plaques de Morgan*."

Personally, I have not observed these angiomas to follow operation, but found them already in evidence in cases of cancer coming under my care for advice and treatment.

Whether these angiomas found in connection with cancer are genuine carcinoderms is a point of great interest, and I hope that these spots will be looked for, now that attention has been directed to them. There is, unfortunately, only too abundant material for making observations, and if such are systematically made it should not be a difficult matter to confirm or discredit this sign.

AUTO-INOCULATION.

Of authentic cases of auto-inoculation of cancer the number recorded is very considerable, and many must no doubt be familiar to you all.

Recently Ebert collected twenty-three cases of contact cancer, such as lip to lip, tongue to gum, one labium majus to another, etc., and mentions the case of a woman who inoculated the corner of her eye from a cancer on the back of her hand.

“CANCER À DEUX.”

In the *Deutsche medizinische Wochenschrift*, of June last, Behla gives a number of instances of “*cancer à deux*,” quoting the names of the observers.

Thus Boas mentions the case of a daughter who inoculated herself with rectal cancer by using the same enema syringe her mother had used during her fatal illness, which was of the same nature.

Tross reports a very interesting and most significant case.

A man developed a carcinoma of the glans penis presenting a structure histologically identical with the cervical carcinoma from which his wife suffered.

Other thirty cases of a similar nature were reported.

Guelliot also has collected twenty-eight such cases.

In my own practice a woman suffering from, and who died from, cancer of the breast, was nursed assiduously during her illness by an apparently healthy woman of about forty-five years of age. This woman developed cancer of the stomach and died from it within twelve months of the death of the woman she had nursed. This nurse was practically in constant attendance upon the case of mammary cancer, and, not being a particularly cleanly person, it is more than probable that she had eaten her food with hands unwashed after dressing the ulcerated sore, or handling the soiled dressings.

ACCIDENTAL INOCULATION IN CONNECTION WITH OPERATION.

Smith cites the case of a London hospital surgeon who developed cancer of the tongue after having accidentally got into his mouth some of the discharge from a cancerous breast.

Budd mentions the case of a French hospital surgeon who died of cancer eight months after having injured himself during an operation on a cancerous patient.

Guermont reports the case of a gynæcologist who developed cancer of the finger at a point where an acne pustule existed, infected during an operation for scraping a cancerous uterus.

Bland-Sutton says that it has been demonstrated beyond possibility of cavil that in women, who have had their ovaries removed for adenomata, it has been found that tumours have subsequently grown in the abdominal cicatrix; such tumours showing, under the microscope, the structure of ovarian adenoma. Since these tumours have been unassociated with any recurrence in the pelvis or secondary nodules in the peritoneum or viscera, the conclusion is irresistible that they were due to infection of the edges of the abdominal incision in the course of the operation of ovariectomy.

Sippel has published a case of cancer inoculated along each one of the suture tracks made after extirpating a cancerous ovary.

No doubt the same local soiling of the edges of skin incisions in operations for cancer, *e.g.*, of the mamma, takes place, and this probably accounts for the presence of recurrence in the form of cancerous nodules so common in the cicatrices of breast cases.

Again, we find often that an extensive operation for

cancer is followed by such rapid recurrence, and such increased energy of growth, that it is evident operation has hastened matters and caused a much worse state of things than non-interference would have done.

Bland-Sutton explains this by suggesting that in the operation the infected blood and lymph vessels, gorged with cancerous material, are divided, and the cancer cells let loose over the damaged tissues, which they infect, and so lead to a still more extensive outbreak of local cancer.

EXPERIMENTAL INOCULATION.

Cancer has also been successfully inoculated experimentally, chiefly, however, in the lower animals.

Langenbeck made a watery emulsion of a soft cancer, mixed it with blood serum, and injected it into the femoral vein of a dog.

Two months later, on *sectio*, nodules were found in the upper lobes of both lungs, and a vascular mass in the middle lobe of the right lung which proved to be cancerous, and was found to be of the same structure as the original growth.

Follin and Lebert used injections made from a cancerous axillary lymphatic gland and, within fifteen days, found in the animal several cancerous nodules in the lungs and liver.

Gonjon has produced melano-sarcoma in small animals within fifteen days after inoculation.

These are but a few examples of many I could quote.

It is most important that much more should be done in experimental inoculation, and it is even more necessary that such experiments should be made on the *genus homo*.

Bosc alludes to three cases of inoculation from man

to man, done both intentionally and successfully, but is discreetly silent about details.

Fortunately there is fairly abundant material for this purpose, although it is at present recklessly wasted annually by the common hangman!

Capital punishment, as at present administered, is so barbarous, so illogical and so entirely non-deterrent, as well as being nothing other than cold-blooded, judicial, murder, that it might very well be discontinued, and the material now lost to science be made available for research in the pathological laboratory. The one thing to fear, however, would be that this committal to the laboratory, instead of the scaffold, would be too deterrent, and, murder becoming a lost art, the material would run short of scientific requirements!

There is a precedent for this source of material for research, inasmuch as inoculation for small-pox was performed experimentally upon six condemned criminals, in 1722, by permission of the government of George I.

No doubt there would be a great outcry from the shrieking sisterhood of both sexes; but they should, of course, be simply ignored, for science must be permitted to pursue the calm and even tenor of her way, undisturbed and undeterred by the vapourings of irresponsible cranks.

In making experimental inoculations two points strike me as likely to help materially towards a successful result if duly observed, *viz.*, that the part to be inoculated should be suitably irritated for a sufficient time, and that the infective material should be taken from an actively enlarging lymphatic gland or metastatic focus, since here we may expect to find the germ

in its greatest activity, and free from the effete material of the primary growth, as well as from other germs.

I cannot but think that one is justified, even at the present time, in saying that, since auto-inoculation and accidental inoculation are so common, and experimental inoculation has been so successful, there should be no longer any doubt that cancer is, in truth, a contagious disease.

CANCER DISTRICTS.

With regard to locality, we find that cancer is more prevalent in some places than others, so much so that the former have been designated "Cancer Fields."

We find the highest death rate from cancer in districts which lie low, and are liable to seasonal floodings, and characterized by alluvium and subsoils of the various clays. The favourite districts in the North and East Ridings of Yorkshire lie principally along the banks of the Ouse, the Derwent, and the Humber. I believe the Derwent region is locally called "The Cancer Valley."

On the other hand, cancer is least prevalent in elevated districts, where there is a good fall for drainage, freedom from floods, and characterized by porous subsoil, and the oldest palæozoic rocks, especially the limestones.

Thus we find cancer most rampant where sewage is most difficult to be got rid of, and where it is most likely to be deposited and remain after floodings or high tides, on a non-porous soil.

This permits of and fosters the prolific growth of micro-organisms; and the frequent occurrence of shallow surface wells in such districts suggests an easy and extensive contamination of drinking water.

It is not difficult, therefore, to realise how cancer may be spread in such localities, and the frequency of its occurrence in the alimentary system favours this view.

CANCER HOUSES AND ROOMS.

As might be expected, we also find in these districts certain houses, and even certain rooms in houses, which seem to be cancer-haunted.

The authentic cases recorded are numerous, but as too much time would be necessary for detailing them I shall quote only one or two instances.

In a house near London a room was occupied by three women in succession who all died of cancer at fairly short intervals. Each of these women appeared to be in perfect health when she in turn came to occupy this room, and had lived in other rooms in the same house; but within a year of occupying this room they developed cancer. There was no relationship between them.

No further cases of cancer occurred in this house after the room was thoroughly disinfected, and the bedding burnt.

There is in Driffeld a row of three notorious houses, or rather hovels, all under one roof, without drainage and with doubtful water supply, where I have attended cases of cancer in each, and in one of these houses more than one case. At present I have a case of cancer of the breast in one of these houses.

There is also a narrow street in Driffeld, undrained and also with doubtful water supply, where cancer is especially common.

It was in one of the houses in this street that the two

cases occurred which I mentioned under the subject of "*cancer à deux*."

Such circumstances as these appear to me to strongly suggest that cancer is infective, and also that locality is a factor in its transmission.

GEOGRAPHICAL DISTRIBUTION.

Cancer seems to be chiefly a disease of temperate regions, avoiding the extremes of temperature such as exist in Greenland or Iceland and the Tropics. Although the extremist cold has no destructive effect upon bacteria or their spores, it certainly keeps them dormant, and this would explain the paucity of cases of cancer in cold climates.

It is not so easy to account for the alleged infrequency of cancer in the Tropics, but it is probably more apparent than real, and may be due to less accurate supervision of disease in these regions. Besides, as a matter of fact, cancer is very common in many parts of India and China.

One reason why so little disease and so few cases of old age are seen among savage peoples, for example in Central and South Africa, is the regular, unostentatious, and mysterious disappearance of such useless individuals, about whose fate no one exhibits any inconvenient curiosity!

Again one need not be surprised to find in the distant islands of the Pacific a healthy native population. They live much in the open air, in an atmosphere practically free from pathogenic germs, so long as contamination from without does not reach them; but the very disastrous results of imported disease, such as small-pox,

measles, syphilis, etc., are notorious, and one can easily believe that the advent of cancer-bearing individuals would be followed by the spread of this disease also.

ETHNOLOGICAL.

The freedom of certain peoples from cancer does not appear to be due to individual immunity, but to the accident of locality and environment and the mode of life.

Under favourable conditions any one may become a victim to cancer.

There is a popular belief that Jews as a race are remarkably exempt from cancer, but this belief is quite erroneous, as is shown by cancer statistics. One reason alleged for this belief is that Jews, generally speaking, have a great repugnance to being inmates of hospitals where Gentiles are in attendance, and, so, few cases are found in these institutions. Private practitioners do not find that Jews exhibit any special immunity from cancer in general. The male Jew may, unquestionably, claim perfect immunity from one form of cancer which his Gentile brother may suffer from, but, apart from this, he is equally vulnerable and liable!

MICROBES IN CANCER.

About fifteen years ago, Scheurlen isolated from cancers of the breast a bacillus which he claimed to be the active agent in their causation. It grows readily in blood serum, and forms a red deposit on potato. It reproduces by spores which stain only by the Ehrlich method, in use for the tubercle bacillus, but the bacillus itself stains by ordinary methods. He has injected

pure cultivations into the mammary glands of bitches with the effect of producing a hard tumour which he states is epithelial.

Doyen lately submitted a paper to the French Academy of Medicine, stating the constant presence of a new microbe in cancerous tumours, which he isolated and cultivated. He says it occurs in the form of motile diplococci, which can be cultivated in tubes of gelatin and gelose with the addition of a special bouillon.

This microbe is more easily found in the affected glands and secondary growths than in the primary tumour, and it is also found in the blood.

To the organism he has given the name "micrococcus neoformans."

In animals, he says, it determines an intense epithelial inflammation followed by formation of adenomata. The subcutaneous injection of sterilized cultures of the organism induces a local reaction in the cancerous growth which he compares to the action of tuberculin on tuberculous foci. The post-operative injection of this liquid has given results satisfactory to Doyen. I daresay we shall hear more of this microbe after further experimentation.

That these micro-organisms are different in structure is no reason for doubting their causal relationship to cancer, for, as in suppuration several different microbes are concerned, so in malignant disease, which exhibits much greater variety than suppuration, we may, *a fortiori*, expect to find several different pathogenic bacteria involved.

HEREDITY.

With regard to heredity in cancer, the believer in the infection hypothesis cannot possibly accept the doctrine

that an individual will develop cancer in later life merely by virtue of his having had cancerous parentage.

It is imaginable that the children of cancerous parents may acquire more or less vulnerability congenitally, as in the analogous case of tubercle; but it is most improbable that the disease itself can be transmitted. If it could be so transmitted we should expect to find it at or soon after birth as is the case in syphilis.

It is interesting to find that even the warmest advocates of heredity in cancer cannot trace cancerous parentage in more than 50 per cent. of cases of this disease.

The occurrence of cancer in several members of a family, after the death of parents from that disease, cannot be accepted as evidence of heredity; but, on the contrary, it can, and ought to, be accepted as evidence of infection from an obvious source.

TREATMENT.

The question of treatment of cancer hardly comes within the scope of my subject, but I am tempted to allude briefly to it.

With our present knowledge this is limited to simple removal of the tumour, if accessible, by the surgeon at the earliest possible moment, and no guarantee can be given by the surgeon that every particle has been removed, or that no recurrence will take place.

But, given an infectious origin, almost certainly bacterial, the lines on which scientific and successful treatment may be carried out become more clearly defined.

Syphilis was long treated empirically. The treatment is still the same but it is no longer empiric, for

the responsible agent is overcome by two of the most powerful bactericides known.

We must find a bactericide which will prove of equal efficacy in the case of cancer, or it may be that serum-therapy will prove effectual. There is even now reason to hope for good results from the use of electricity, whether in the form of Röntgen rays or currents of high potential, both of which are alleged (Cohn and Mendelssohn) to be inimical to bacteria.

As regards prophylaxis, much may be hoped for from notification; improved sanitation, including disinfection of houses, cremation of bodies, destruction of dejecta, dressings, etc., by fire; the use of pure drinking water; scrupulous personal cleanliness, especially the avoidance of unwashed hands when food is taken, the use of the Turkish bath; exercise; moderation in diet; abstinence from alcohol in excess; and general observance of the known laws of health.

It seems to me that, after all, my trying to hold a brief for the infection hypothesis of cancer is a work of the purest supererogation, since it must be evident that it is hopeless to attempt to explain the causation of cancer on any other ground.

No alleged cause can possibly be accepted which is not universally applicable, and infection from without is the only suggested cause which will satisfactorily account for every case of cancer.

To sum up, this is my case:—

From the evidence at my disposal, I deduce that cancer is a specific disease, that it is contagious and therefore infectious. That there is an infective agent is a logical *sequitur*.

Probability and analogy point to this agent being a

microphyte and not a microzoön. That this microphyte is a facultative aerobic bacterium is suggested by the fact that, though it grows fairly well under free access of air, it grows very much better without it. This is well exemplified by the striking difference in behaviour of epithelioma of the lip and of the tongue. Although these parts are very near neighbours, the growth in the one instance is extremely slow, while in the other it is exceedingly rapid. The epithelioma of the lip is exposed to light, to the air, to low temperature, and there is an absence of moisture. The epithelioma of the tongue, on the other hand, is situated in an ideal culture chamber, in the dark, where there are moisture, a fairly constant favourable temperature, and exclusion of air.

Since a specific disease can originate only from a specific cause, all other alleged causes can only bear the relationship to cancer of, at most, the condition precedent.

The proof rests in the hands of the experimental pathologist, supplied with material by the practical clinician.

The time is more than ripe for combined and determined effort to investigate this subject, an effort which must be tirelessly persisted in until the problem is finally solved.

There are few who have not suffered in person or friends from this grim and terrible disease, and it is certain that every one will wish well to the search for the cause of cancer, and no one more than our genial and royal colleague, our august Sovereign, King Edward, who has already referred to the subject in most emphatic terms.

One great obstacle to investigation is absence of the sinews of war; we must have money and plenty of it if we are to hope for a successful issue.

It is hardly fair to look for help to the liberality of private individuals alone, as was recommended by the Prime Minister the other day, although some multi-millionaire might easily less worthily dispose of a half or quarter million than hand such a sum over to the conjoined Colleges of Physicians and Surgeons for this purpose. It is the bounden duty of the State, and it ought to be considered a privilege, to grant, through the Government, a generous subsidy for a cause having as its object the benefit of the Commonwealth.

This country has had an example set by Germany and the United States, who have both set apart large sums of money for the investigation of the cause and nature of this disease which it would be well for England to follow.

Another obstacle, and it is a still greater one, is the supineness, the indifference, the utter apathy displayed by the members of the medical profession in general, who appear to be fettered by a paralysing fatalism. Let us rouse ourselves from this state of lethargy and by a determined, unanimous and sustained effort remove from the science of medicine this most discreditable reproach.

Germany can claim the honour of having discovered the cause of tuberculosis; let it be to Great Britain that the honour of the elucidation of cancer shall belong, an elucidation which shall earn the undying gratitude of all mankind, and establish for Albion a glorious fame which shall be imperishable.

THE EXOGENESIS OF CANCER.¹

GENTLEMEN,—I make no apology for again introducing the subject of the ætiology of cancer. The elucidation of this disease is, or ought to be, the burning question of the day. When we consider the number of victims it annually hurries to the grave after a period characterized by great bodily suffering and mental depression; the dread of its advent by those not yet attacked; and the reproach which it undoubtedly is to the science of medicine, the duty is obviously incumbent upon the medical profession to make every possible effort to discover its cause and cure. We have a personal as well as a scientific motive in trying to make this discovery, for although we are medical men, we do not on that account possess a prophylactic talisman to confer upon us exemption from cancer, and therefore we are just as liable as other people to contract it, and even more so from our coming more frequently in contact with it than members of the laity generally.

I do not propose to-night to discuss the many theories and suggested causes of cancer which have been from time to time promulgated and found insufficient, but shall confine myself to bringing before you evidence of its exogenesis.

¹ Thesis read before the East Yorks and North Lincoln Branch of the British Medical Association on March 20, 1903, with a view to eliciting a discussion on the subject, with subsequent additions.

The term "cancer" is used throughout, generically, to include all that is clinically understood as "malignant"; also the wider term "infection" will be understood to include the more restricted one of "contagion."

I presume it will be freely admitted that, in making a diagnosis, if any one point is absolutely inimical to it that diagnosis must be discarded. For example, however closely neurasthenia may simulate Landry's paralysis, if the reflexes are intact, then Landry's paralysis must be excluded; and conversely, however anxious one may be to consider a case of Landry's paralysis to be one of neurasthenia, if the reflexes are gone, then the more favourable diagnosis must, of necessity, be abandoned. In like manner I claim as a postulate that, *for the alleged cause of a disease to be acceptable, it must necessarily be of universal applicability. In other words, if any alleged cause entirely fails in any one case, then that cause cannot be the true and exclusive one.* My contention, and it is also my implicit belief, is that cancer arises from without the organism by infection, and that infection occurs only under certain favourable conditions which render the organism vulnerable, *i.e.*, that a *condition precedent* must be established, produced by irritation, occurring within or without from any cause; or by injury; or by degeneration of tissues from obsolescence or senility; or by chronic disease; or by congenital susceptibility; and that no other hypothesis will satisfactorily explain the incidence of cancer in every case. I cannot, therefore, admit as tenable such alleged causes as uric-acidæmia, the influence of arsenic, excessive consumption of flesh or of common salt, &c.; or any of the theories such as Cohnheim's, Hanseemann's, Thiersch's,

&c., for not one of them is applicable to each and every case. At the same time, while utterly rejecting such alleged causes as untenable, I freely admit their possible connection with cancer, but only in so far as they may induce, or help to induce, a condition precedent.

WHAT FACTS ARE KNOWN ABOUT CANCER, AND WHAT MAY BE LOGICALLY DEDUCED FROM THAT KNOWLEDGE ?

We know that cancer is a specific disease, and therefore it must arise from a specific cause.

We know that it is intensely infectious to the individual, and therefore it must be capable of infecting others.

We know that it propagates itself by infection of its immediate environment and by metastasis, and that metastasis is the chief agent of dissemination in many other germ-caused diseases.

We know that cancer is pre-eminently a human disease, and that it occurs only in such of the lower animals as are intimately associated with man, and that it is practically unknown in wild animals. This may fairly be looked upon as very strongly suggestive of contagion.

We know that cancer has favourite sites and favourite tissues (the epithelial), all easily accessible from without, and many of them are ideal culture chambers.

We know that cancer haunts favourite localities which are all of the same character, and favourable to the harbourage and growth of bacteria.

We know that irritation of some sort is closely associated with cancer, so much so that it is recognized as practically always precedent, thus preparing the soil for the reception of the infective agent.

We know, also, that cancer is purely and wholly a local disease at the outset, and that any success in surgical treatment has been attained only by early operation, and that operation in advanced cases is only palliative, and not always that. This initial local condition is strongly suggestive of contagion from its resemblance to other germ-caused diseases.

We find in cases of cancer, when the disease has become well established, a well-marked cachexia similar to what is observed in the later stages of chronic infective diseases.

While cancer is strictly analogous to no other single disease, admittedly germ-caused, it is analogous to many of these diseases in some one or other of its features, with the exception of one. This exception is the peculiar and characteristic nature of its metastases. These are said to mimic the structure of the primary growth, but there is no mimicry here. They are histologically identical in structure with the primary tumour, which indicates that migration of the cells of the original growth occurs, as well as of the infective particles.

This migration of epithelial cells is generally looked upon as extraordinary, and is even used as an argument against the exogenesis of cancer; but there is nothing wonderful about it, for the very structure of cancerous tumours favours and induces it. The cause and structure of these metastases are evident when their origin is understood. A malignant growth *arises* in the first instance from a cell or cells, under the influence of a stimulus, more than probably external, taking on autonomy and proliferating actively. It *consists* simply, in the case of the epitheliomata, of epithelial cells lying

more or less loosely in meshes or alveoli of connective tissue, called stroma, to which they are not in any way attached, and which does not pass between individual cells. Lymphatic channels communicate freely with the alveoli, in fact the alveoli may be regarded as dilated lymph spaces which are the radicles of the lymphatic trunks, and these latter lead to the lymphatic glands. Thus the epithelial cells are bathed in the lymph, and being dislodged by their own overgrowth, or of their own free will, they cannot help entering the lymphatic stream. Blood-vessels run in the stroma and are often dilated, and being invaded by the actively proliferating cells, the latter enter the general blood circulation.

In the case of the sarcomata, the growth consists chiefly of cells which are derived from connective tissue, and are embedded in a stroma which is intercellular and closely connected with them. The smaller blood-vessels are in direct contact with the cells, their walls being often formed of nothing but the cells of the sarcoma, a single layer of endothelial cells separating the blood from the tumour cells. Thus it is easy for portions of the growth to be carried away in the blood stream. There are no lymphatics in sarcomatous tumours. These living, infective, autonomous cells, carried away by the blood and lymph streams, as emboli, on becoming impacted, establish new malignant colonies by the active proliferation of the cells themselves and the reproduction of their contained germs. These metastases in turn repeat the process, until at length the organism is overwhelmed and overcome by their malignant action.

This migration of autonomous malignant cells has its parallel in the migration of normal cells. For example, healthy osteoblasts, under the influence of some stimu-

lus, probably mechanical, break adrift from their moorings and, coming to rest in muscle substance, found, in the interfibrillar connective tissue, a flourishing colony of bone, and this is known to the pathologist as "myositis ossificans."

WHAT IS RECORDED OF CANCER?

In my address on the ætiology of cancer I have given instances of *cancer-à-deux*, of auto-inoculation, of accidental and operative inoculation, and also of experimental inoculation, quoting reliable authorities, and I need not repeat them here. I have also given instances of cancer-haunted districts, houses, and even rooms reported by careful observers.

Since reading my address in May last, I have received the presidential address of Mr. Nash of Bedford, president of the South Midland Branch, on the subject of cancer in North Bedfordshire. He records no less than thirty cases of *cancer-à-deux* and cancer-houses occurring in his district alone. He also quotes from Dr. Behla's investigation into the infectious origin of cancer, which is so interesting and significant that I repeat it here.

"The town of Luckau, in Bavaria, consists of a central main portion with 3,000 inhabitants, flanked on the east and west respectively by sub-divisions of the city called Kalau and Sando, each with a population of 1,000, making 5,000 in all. In twenty-two and a half years (1875-1898), no cases of cancer occurred in the western suburb, Sando; cases were not infrequent in the central main town, and 73 deaths from cancer, out of a total of 663 deaths from all causes, occurred in the eastern suburb, Kalau. Cancer therefore caused 1

death out of 9 in Kalau against 1 out of 25 or 30 in the entire town, whereas no cases occurred in Sando. During the twenty-two and a half years the number of inhabitants and their habits of life remained the same. The population is agricultural and lives on the products of its own gardens and fields. The dwellings are similar in size. The soil of Kalau and the central town is flat, low and moist; that of Sando elevated, sandy and dry. A stream or ditch closely encircles the central town and Kalau. Cancer followed the course of this ditch. In Kalau all the gardens are watered by it.

“Of the 127 houses in Kalau 56 were cancer-houses; 45 had a single case, 10 two cases, and 1 four cases. Behla attributed this unequal distribution of cancer to the location of the ditch. In the cancer suburb all the gardens were watered from it, and the people were in the habit of rinsing vegetables in the water from it, which is stagnant and foul. Behla believed that the vegetables were infected from the water of the ditch, and the people by the vegetables, large quantities of which were eaten raw. Behla considered that a parasite must be the cause of this irregular distribution of cancer.”

Can any reasonably intelligent being, after reading such evidence as this, hesitate for a moment to admit the extreme probability of the external origin of cancer? If anyone remains unconvinced let him apply the touchstone of these statistics to any other suggested theory of the causation of cancer. Think for a moment of the miraculous assembling of the hypothetical embryonic rudiments in Kalau and their total avoidance of Sando; think of Kalau's selfish monopoly of all the available spermatic influence of cells; think of the deplorable

amount of unconscious evil memory of the tissues exhibited by the inhabitants of Kalau; think of the extraordinary amount of wear and tear of the unfortunate people of Kalau, which is requisite to induce the too rapid growth of their cells and consequent degeneration necessary to the development of cancer, and how placidly the people of Sando must spend their existence; then we must presume that Kalau is given over to excessive flesh eating, uricacidæmia, the excessive consumption of common salt, and to the malign influence of arsenic, while Sando, on the contrary, must be vegetarian, shunning salt, and be free from the evil effects of arsenic.

It is only waste of time to pursue farther this *reductio ad absurdum*, and it must be clearly evident that only one explanation of Behla's statistics can be tenable, and that is what he suggests, viz., infection from without.

THE CHANNELS OF INFECTION.

Since the favourite site of epithelial cancer is some part of the mucous membrane, the mouth and respiratory passages suggest themselves as very obvious channels. The very objectionable fashion of long skirts, which sweep the filthy, germ-infected streets, and the open and loose arrangement of their nether garments, suggest another obvious channel of entrance in the case of women, who notoriously suffer from cancer of the generative organs. Again, when one considers the enormous number of the sweat tubes whose calibre is immense in proportion to the excessive minuteness of micro-organisms, the wonder is that we ever escape any germ-caused disease, for our skins must be fairly full of germs in spite of the ordinary methods of cleansing.

Charles Creighton, in a monograph which he has lately published, entitled "Cancers and other Tumours of the Breast," claims to have discovered their true seat and anatomical cause. He states that mammary tumours do not arise from the breast-gland proper, as is generally supposed, but from the large sweat glands of the mammary skin.

With this interesting pathological point I am not tonight concerned, beyond accepting the opportunity it affords of drawing attention to this confirmation of the sweat tubes being a channel of infection, and to the explanation it offers of the great frequency of mammary cancer, while at the same time it commends itself to me as an argument in favour of the external origin of cancer. Once admitted to the organism by any channel a germ can easily find its way to any part of the body, and where vulnerability exists from any cause, there it can initiate malignant disease.

CARCINODERMS.

I took the liberty of introducing a new term in connection with cancer, viz., "Carcinoderms," to describe the cutaneous angiomas found so often accompanying cancer, especially of the breast. It has been maintained by many that such angiomas are not pathologically connected with cancer, but that they occur quite independently of it. The angiomas, however, described by de Morgan, Leser and myself are *sui generis*. There are not infrequently to be found in apparently healthy individuals, angiomas of the skin, some even congenital, scattered irregularly over the body and extremities, but they are few in number and small in size, and are no more the typical angiomas found, for example,

clustered many and large round a cancerous mamma, and which once seen can be neither forgotten nor mistaken, than the pustules of acne on the forehead and chest are identical with the pustules of variola, although the former have been mistaken for the latter. Moreover, these angiomas have been observed to appear after operation on the breast and were rightly considered of bad omen. I make no dogmatic assertion that these angiomas are genuine carcinoderms, but I consider that their presence in certain circumstances is of very sinister significance. I only suggest their highly probable direct pathological relationship to cancer. I fully described these skin manifestations in my address, so that I need not now waste time in repetition.

HEREDITY.

With regard to heredity there is no evidence that transmission of the disease itself has ever occurred. Even in the case of women suffering during pregnancy from cancer of the uterus itself, the children born of such mothers have not been known to have contracted the disease. Nor can the children of cancer-free parents, who may subsequently contract the disease, be expected to inherit what their parents did not at the time possess, and therefore could not bequeath. The occurrence of cancer in several members of a family, after the death of parents from that disease, does not necessarily point to heredity so much as to infection from a very obvious source. Suppose, however, that an infant is born with a cancerous tumour of a cancer-free mother, as I believe has occurred, how can the incidence of the disease be accounted for? To my mind such a case

would indicate infection from without, the germ which has gained access to the parent in some way, having finally come to rest in the foetus instead of the mother, who is relieved of the cancer by the natural process of parturition, instead of artificially by surgical operation. The warmest advocates of heredity cannot muster more than 50 per cent. of cancerous parentage, which means that the evidence, even according to them, is exactly as much against heredity as it is in favour of it. At the same time, nothing like this percentage is admitted by pathologists, indeed the question of inheritance is rapidly becoming entirely disregarded. I presume no one would seriously allege that scarlet fever, measles, influenza, &c., are hereditary, and yet it is a fact that the children of parents who have had these diseases also suffer from them! It is notorious, however, that some children are much more susceptible to infectious diseases than others, and the former probably have inherited from their parents a congenital susceptibility. The most that I am disposed to concede to heredity is that cancerous parentage probably confers a congenital vulnerability beyond the normal, such as occurs in the case of tuberculous parents, nothing more.

PROPHYLAXIS AND TREATMENT.

This subject hardly comes within the scope of my thesis, but I introduce it because it has a direct bearing on the hypothesis that cancer is an infectious disease.

With regard to prophylaxis against cancer, the keynote is scrupulous cleanliness, in its widest application, as it likewise is in the case of all dirt diseases. Personal cleanliness is, in my opinion, best attained by the fre-

quent use of the Turkish bath. The hot, dry air of this bath causes perspiration to ooze freely from every pore, carrying with it any impurity lodged in the sweat tubes, germs included. Great thirst is naturally produced, which demands the imbibition of cold water in abundance. Following on this, perspiration becomes still more abundant and free, from the absorption of the water. Now this water has been absorbed by the capillaries and venules of the mucous membrane of the stomach, and having thus entered the blood it is carried through every organ and every part of the body, so that before reaching its outfall on the skin in the form of sweat, it has previously irrigated the entire organism from centre to periphery. The subsequent massage and thorough washing down with hot water and soap, followed by a cold plunge, turns out the bather clean, both within and without.

A very important point in prophylaxis is that food should never be taken with unwashed hands, and vegetables which are to be eaten raw should be most thoroughly cleansed by scrubbing, &c.

Notification should be adopted, for this would enable precautions to be taken against the spread of the malady, and would afford more accurate information as to the localities where the disease arises than can be obtained from statistics as to the places of death from cancer. Notification should be followed by disinfection of infected houses, bedding, clothing, &c. Cremation of bodies, dejecta and dressings should be practised. The purity of drinking water should be ensured.

In the absence of a demonstrable micro-organism there is little hope of the preparation of an antitoxin,

nor does the experience with that prepared from the tubercle bacillus hold out much hope from the serum treatment of cancer.

I believe the use of electricity in the various forms of Roentgen rays, Finsen light, currents of high frequency and potential, has been found beneficial in certain forms of cancer, and it is possible there is a more extended future before this method of treatment.

The successful treatment of syphilis by two of the most powerful antiseptics we possess, suggests hopefulness of similar success in the treatment of cancer from a medical point of view.

Is it Utopian to suggest that some bactericide, for example, salicylic acid in the form of salicylates, or formalin, which latter has, I believe, been successfully employed in septicæmia, freely diluted and imbibed during repeated Turkish baths, and so brought into intimate contact with cancerous tumours throughout the body, through the medium of their blood-supply, may have a beneficial effect? This method, I venture to submit, is worthy of experimental employment.

STATISTICS OF MY OWN PRACTICE.

I have been requested to give the cancer statistics of my own practice, and I have pleasure in stating them generally. I must, however, suppress the more interesting items of cancer-houses, &c., for my allusion to such in my address was strongly resented by the local fathers. I may state that during 1901, as reported by the Medical Officer of the East Riding County Council, the death-rate from cancer, for the town in which I practise, was twice the average death-rate from this disease for the whole county. I have not seen the report

for the year 1902, but I hope and believe that the death-rate from cancer will not be so high.¹

During almost twenty years of practice in town and country, I have attended 113 cases of malignant disease, of which 104 have died, two have left the neighbourhood, and seven remain under observation. Seventy-six died in the town and twenty-eight in the surrounding country. Thirty-seven were males and sixty-seven females. As is usually the case, cancer of the alimentary tract and accessory glands yield the highest percentage, viz., 57 per cent., the reproductive system follows with 21 per cent., the breast was affected in 14 per cent., and other parts in 12 per cent. Fourteen were operated on, including one case of cerebral neoplasm. The greatest number of deaths in any one year was ten, in 1890, eight each in 1892 and 1897, and seven in 1886. The smallest number in any year has been three. These figures of course apply to my own practice alone, and are independent of those of my fellow medical practitioners, which I am unable to supply, and I may say that I have no monopoly of cases of cancer.

OBJECTIONS TO THE INFECTION HYPOTHESIS.

I should like to mention a few objections to, and arguments used against, infection and exogenesis which have been made to me. Several of them should not be

¹ The Report of the Urban Medical Officer of Health for March, 1903, states that of the twelve deaths for the month three were due to malignant disease, "which is a high percentage." He concludes his report by saying: "I am of opinion that cases of phthisis and malignant disease should come under disinfection as well as the notifiable diseases."

I presume it was in accordance with this view that the Inspector of Nuisances was directed to disinfect a bedroom after a fatal case of cancer. I need hardly add that this is a wise and sensible proceeding, as well as a highly enlightened one.

considered seriously, were it not that they may prejudice and even deceive the unwary.

(1) *Cancer cannot be an infectious disease, because the infectious germ has not been found.*—This is obviously merely begging the question. Non-discovery and non-existence are not synonymous terms. Further, the same objection may be made equally in the case of scarlet fever, and many other diseases admittedly infectious.

(2) *There is complete absence of all proof of real infection.*—This objection can only be made by him who is either entirely ignorant of the literature of cancer, or who resolutely shuts his eyes to the evidence of those who have collected and recorded many cases of genuine and undoubted infection, and whose scientific status is beyond cavil.

(3) *Cancer is not strictly analogous to any known infectious disease.*—It is not, why should it be? Every infectious disease has its own peculiar characteristics and its own peculiar germ; and every pathogenic germ has its own peculiar and characteristic malign influence. One might with equal justice say that radium cannot be a metal, because it is not strictly analogous to any other known metal.

(4) *All infectious diseases have a tendency to self-termination, whereas cancer is persistently progressive.*—This is, of course, a pure fallacy. All infectious diseases do not tend to self-termination. Both tubercle and leprosy tend notoriously to be progressive, although, in common with cancer, cases of these diseases have been known to completely disappear spontaneously.

(5) *In a disease so common as cancer, more cases of*

cancer-à-deux would be expected, while they are so rare as to be explicable by coincidence.—This is simply a question of lack of observation. The rarity is due to the fact that such cases are not looked for. Cancer arises in no happy-go-lucky fortuitous manner. If there is any truth in my contention that cancer arises by infection from without, then every case of cancer is one of *cancer-à-deux*, mediate or immediate. Again, co-incidence cannot possibly account for the case recorded by Tross, of a man who suffered from cancer of the glans penis, showing a histological structure of uterine-cervical epithelial cells. Such a case as this, and it is not a solitary one, for over fifty-eight such have been recorded, is alone sufficient to prove these three points: The infectivity of cancer; the external origin of cancer; the inocubility of cancer in man.

(6) *There are very many kinds of tumours which differ so much from each other that a different germ would be required for each.*—This is the merest quibble. Clinically there are only two classes of tumours, viz., the benign and the malignant. The former are for the most part simply local hypertrophies of normal structures and tend to remain so, and they do not form metastases. Benign tumours therefore do not require any specific germ to originate them, simple stimulus of a mechanical nature being quite sufficient in many cases for the purpose. They are comparable to the pearl of the oyster, which is simply a deposit of a normal substance around a foreign body. Malignant tumours are of two kinds, differing in origin but alike in character. They are those arising from epithelium and called epitheliomata, and those arising from connective tissue and known as sarcomata. All other difference in form

and structure simply depends entirely on the tissue of origin and the proportionate relationship of cells to stroma. The old notion that there is a special cell indicative of cancer is quite erroneous. Malignant tumours all behave alike, infecting their environment, tending to ulcerate, forming metastases and eventually destroying the organism. Such being the case, one germ for each of these two classes is quite sufficient, by attacking the various tissues under the favourable conditions already stated, to initiate malignant action; and since it has been found that the same germ may produce totally different diseases in different plants (as pointed out by Mr. Jonathan Hutchinson, in the *Lancet* for August 31, 1901), there is no reason to doubt that one germ alone is capable of initiating malignancy in every case.

(7) *Tubercle and leprosy are destructive diseases, while cancer is constructive.*—This is another fallacy. All these diseases are at first constructive, as all tumours are. Nodular leprosy is markedly constructive and tends to remain so. Rodent ulcer, which is malignant, is destructive from the outset. Again, malignant tumours, at first constructive, rapidly tend to become destructive, for by their hasty and ungoverned overgrowth, they cut off their own blood-supply and so initiate a suicidal necrosis, which is completed by the germs of suppuration.

(8) *Why should benign tumours become malignant?*—Why should they not? Consisting as they chiefly do of local hypertrophies of normal structures, they are obviously equally liable to infection, after irritation or traumatism, with the tissues themselves from which they spring. In certain situations, too, by their very overgrowth they, like malignant tumours, also cut off their

blood supply and so induce necrosis, and where the germs of suppuration easily gain admission cancerous germs can equally easily do so.

(9) *Sarcoma has been observed to follow removal of a benign fibroma from a tendinous or periosteal structure, the malignant change being due to degeneration of tissue.*

This doctrine of degeneration is made very free use of by the non-believer in infectivity, and besides being entirely hypothetical it does not fulfil the postulate I claimed at the outset of my thesis. A witty patient of mine calls influenza the "doctors' big umbrella," because it is the term used to cover many diseases which are not diagnosed. "When in doubt call it influenza"!! When the non-believer in exogenesis of cancer can suggest no other reasonable cause for cancer he falls back upon degeneration of the tissues.

Degeneration, as I have already pointed out, is one of the factors in establishing the condition precedent, but it cannot *per se* initiate cancer. It is most unfortunately true that cancer very often indeed attacks persons in the very prime of life, with no degeneration in particular going on, but in them the necessary condition precedent has been established by other means. In the case in point surgical traumatism was just what was required to prepare the soil for invasion by an external infective agent, and the surgeon, by interfering with a benign tumour with of course the best intentions, had all the same done his patient unintentional harm.

(10) *Embryonic rudiments, or cell-rests, become active after many years and originate cancer, so that no germ is necessary.*—This theory is as hypothetical as the rudiments themselves. The nearest approach to

such shadowy rudiments is the dermoid, which, however, consists of natural epithelial elements gone astray in development, and does not tend to become malignant.

(11) *Cancer does not appear in epidemic or endemic form.*—It does not occur in epidemic form certainly, which is something to be thankful for; but that it appears in endemic form is notorious, as evidenced by the statistics of Kalau and such significant terms as “the cancer valley.”

(12) *The deaths in so-called cancer-houses are so far apart in point of time as to have no significance.*—This objection indicates considerable want of familiarity with the literature of the subject, and is best met by the quotation of a few instances out of the very many recorded, which to any reasonable person must be of the greatest significance.

(a) Dr. Scott (*British Medical Journal*, vol. i, 1894, p. 1,302), relates that J. K., aged 50, died of cancer of the liver; J. L., aged 54, succeeded him, and died two years after from cancer of the bladder; A. L., aged 60, was then appointed, and died in eighteen months of cancer of the stomach. These three men all inhabited the same room in turn, and slept in the same bed, which was a walled-in one. They were all strong and well when they came to live in this room. They were not related and they had no history of heredity.

(b) Dr. Collins supplies Mr. Nash, of Bedford, with the following case: S. S., aged 64, died in May, 1897. Her brother, E. S., aged 81, died in October, 1899, and his wife in July, 1898. The three died in the same house of cancer of the stomach, within three and a half years.

(c) Mr. S. Phillips quotes the following case: Mrs. S., aged 68, died in November, 1897, in house 78 B., from cancer of the stomach. Her daughter, Mrs. S., aged 44, died from cancer of the uterus in March, 1898, and the husband of the latter was operated on for epithelioma of the lip in the same year. These three persons were all healthy when they went to live in this house.

(13) *Experimental inoculation in lower animals has given negative results.*—So it has in many cases, but this objection, preferred in the face of the many successful experiments vouched for by reliable men, does not prove that inoculation cannot be successful. All that it can prove is that in these cases the successful method was not employed.

In order to be successful in experiment one should imitate as closely as possible what occurs in the cases of cancer which we meet with.

(a) Since cancer is pre-eminently a human disease the best subject for experiment would naturally be man himself. Such experiments could be made by enthusiastic self-provers, or on voluntary subjects, or on condemned criminals. Precedent for this latter method is found in the reign of George I, in 1722, when six condemned criminals were permitted to be inoculated with the virus of small-pox by the Government of that time; and lately a criminal in the Sandwich Islands was inoculated with leprosy tissue in several parts of his body, as described by Arning. Failing man himself the animals should be as anthropoid as possible, and therefore the highest apes would be the most suitable.

(b) I consider that it is a *sine qua non* for success that a condition precedent shall exist; for this can be

traced in every case of cancer if it is carefully sought for. It seems to me to be hopeless to expect successful results, for example from feeding perfectly healthy animals upon cancerous tumours, for the intact mucous membrane of the alimentary tract is probably invulnerable. If, however, the mucous membrane of the stomach and intestines is irritated or injured, by giving at the same time spicules of bone, small pins or tacks, or fragments of glass, the soil would be prepared, and inoculation rendered possible.

Again, the tongue might be suitably prepared by breaking a tooth or two, here and there, so as to irritate and abrade it, and then the cancerous material might be rubbed in from time to time.

Suitable and sufficiently long-continued irritation should also be employed before attempted inoculation of other sites, such as the vulva, vagina, os uteri, anus, &c.

(c) I think the most suitable material for inoculation would be got from an actively enlarging metastatic tumour or lymphatic gland, since here we might expect to find the germ in its greatest activity and free from other germs and the effete products of the original growth.

(d) The inoculation should be immediate, and while the material is still warm, from the subject supplying the cancerous material to the animal to be experimented on.

(e) The tissues chosen for experiment should be derived from the epiblast and hypoblast, since cancer prefers epithelial surfaces.

Senn, of Chicago, who is an opponent of the infection hypothesis, had the pulp of a cancerous gland inserted

into the subcutaneous and muscular tissue of his forearm, and, when no positive result occurred, emphatically asserted the non-infectivity of cancer. Here, however, the cancerous material was grafted upon mesoblastic tissue, which may be considered unsuitable soil, and there was no proper condition precedent inaugurated, nor can one negative experiment be considered conclusive. Messrs. Ballance and Shattock implanted grafts of tumours in the healthy tissues of lower animals in a similar way, with a like unsuccessful result, and probably for the same reason.

(f) Cancer is rare in the young, and therefore one can hardly expect, reasonably, to meet with success in inoculating young animals. The animals chosen should be in the latter third of their lives, *i.e.*, of such an age as would correspond to the favourite age of incidence of cancer in man.

(g) Animals should not be killed for at least six months after experiment on internal parts, such as the stomach and intestines, or when intravenous injections have been made. The more superficial parts, such as the tongue, anus, vulva, &c., would be easily under observation at all times.

(h) I do not think that experimentation with the blood or its serum, or the lymph, taken from the vicinity of cancerous tumours, or the blood from the general circulation of persons showing well marked cachexia, has been exhaustively tried.

Such are a few ideas which seem to me worthy of consideration in further experimentation, for that cancer is transmissible to the lower animals seems proved by the simple fact that it does occur in domesticated animals, for example, the dog.

Budd has reported the instance of a pet dog which contracted cancer of the tongue after licking the cancerous lip of its master.

In the *British Medical Journal* for January 31 last there is a leaderette treating of the views of Professor Lubarsch of Posen, who opposes the infection theory on the following grounds:—

(a) No analogy from studies of diseases of plants and animals has up to the present been brought to the support of the theory.

(b) The results of statistical, epidemiological, experimental and clinical researches, have not furnished arguments on the side of the theory.

(c) It has not been shown that any organ is capable of producing cancerous or any other autonomous new growth.

With regard to the first two of these objections Professor Lubarsch simply denies what has already been asserted and even shown to be true by many observers of equal standing with himself.

His third objection is not only no objection at all, but is actually, on the contrary, a powerful argument in favour of the external origin of cancer. It is tantamount to stating that autogenesis of cancer by the organism is impossible, and this is what I have consistently maintained throughout.

It is utterly unreasonable to expect any intelligent person to believe that the cells of any given part of the body which have hitherto behaved in a normal and law-abiding manner for, say, half a century, should, without rhyme or reason, suddenly break out into a state of wild anarchy, and running amok in the body, should

create disaster wherever they go, which eventually ends in the destruction of the organism.

It is imperative that there must be an external stimulus which starts these cells on their wild and malignant career, and it is only reasonable to assume that that stimulus, coming from without, is an infective particle of some kind charged with its characteristic malign influence.

The ingenuity of the opponents of the infection hypothesis will no doubt suggest many more objections, but such as I have quoted are sufficient to indicate their methods.

I now offer you, on the other side, the views of two men whose opinion is deserving of your respectful consideration.

Bland-Sutton says: "There are many facts which indicate that cancer is induced by micro-parasites, for those glands which are direct communications with the air or intestinal gases are most prone to become cancerous, *e.g.*, the mamma, rectum, and stomach, whereas cancer of the thyroid and prostate is unusual. The great frequency of cancer in the cervical endometrium, in comparison with its infrequency in the corporeal endometrium and its extreme rarity in the mucous membrane of the Fallopian tubes, are significant facts in relation to invasion by microparasites."

He says also in reference to the condition precedent: "It is a significant fact that cancer is more prone to arise in glandular organs which have been injured, or are the seat of chronic disease, than in those that are healthy. This is borne out especially in the case of

cancer arising in the neck of the uterus, for this disease is almost exclusively confined to women who have been pregnant, and in the thyroid gland, for cancer of this gland is much more frequent in countries where goitre is endemic."

C. A. Ballance, after detailing certain unsuccessful experiments in inoculation of lower animals made by himself in conjunction with Mr. Shattock, says: "The theoretical considerations in favour of the micro-parasitic nature of cancer, in my judgment, remains as cogent as ever. The parasitic doctrine recommends itself as bringing the essential pathology of malignant growths into natural relation with other diseases, the parasitic pathology of which admits of scientific proof. The natural history of cancer, its auto-inoculability, and the facts relating to its distribution, all point in the same direction; and, notwithstanding the fact that no positive demonstration of the living nature of the virus is yet forthcoming, I cannot doubt that such a demonstration will eventually be achieved, and I venture to submit that no other hypothesis hitherto advanced is capable of giving an adequate explanation of the pathological phenomena of this disease."

For my own part I am satisfied that the exogenesis of cancer is clinically and logically proved, and that the discovery of a causal micro-organism, fulfilling the law of Koch, is only a matter of time. As logical proof I beg to submit these two syllogisms: (a) All diseases infectious to the individual are infectious to others. Cancer is infectious to the individual, therefore cancer is infectious to others. (b) All diseases infectious to the individual have an external origin. Cancer is infectious

to the individual, therefore cancer has an external origin.

In my address I have stated my reasons for considering the infective agent to be a microphyte rather than a microzoön, and also for believing that such microphyte belongs to a certain class.

The great and desirable end to be achieved now is the acceptance of the fact that cancer is, in truth, an infectious disease, so that prophylaxis at least may be carried out. The first and most important step to take is the adoption of compulsory notification of all cases of malignant disease, and their subsequent thorough investigation. This latter can be undertaken by the medical practitioner, while it may be safely left to the experimental pathologist to capture the elusive *contagium vivum*.

THE CAUSATION OF CANCER.¹

THERE is no subject of more engrossing interest at the present time to the pathologist, the clinician, and the public generally than the problem involved in the elucidation of cancer. The crux of the whole matter is the discovery of the *causa causans*. That there are many contributory causes is very evident but there is, and can be, only one ultimate cause.

In considering this cause there is a postulate which must be unhesitatingly admitted, viz., that any alleged cause to be acceptable must be absolutely of universal applicability.

Of all the theories hitherto advanced and causes suggested—and they are legion—only one fulfils this postulate, but it does so completely. This one is the theory of the external origin of cancer, *i.e.*, that cancer is an infectious disease.

That the belief in the infectious nature of cancer is rapidly becoming widely held, not only by medical men, but also by the public generally, is undoubted; so much so indeed that the great question now is, “Is cancer infectious or is it not?”

Thus we have two opposed factions, one consisting of those who are out-and-out believers in, and advocates of, infection, of whom I am one; and the other of those who equally strenuously dissent from this belief. There is, no doubt, another class, which, however, may be

¹ From the *Practitioner* for October, 1903.

disregarded as a negligible quantity, typified by that dilettante agnostic, the man with the "open mind," who knows nothing, who believes that nothing is known, of the causation of cancer, and whose Gallio-like attitude is well calculated to delay indefinitely all progress in its elucidation.

The advocate of infection believes that he has strong grounds for his faith and that he can uphold it by clinical and logical proof. The opponent of infection, on the other hand, simply denies that cancer has an external origin. He does not, and cannot, suggest any other satisfactory cause, for not one other single suggested cause fulfils the inexorable postulate—that of universal applicability. He confines himself to stating objections, some of which are pure fallacies, while others are too frivolous to be seriously considered.¹

There are, however, objections advanced which are worthy of serious consideration and, because they are founded upon a want of appreciation of the facts of the case, it is the purport of this paper to discuss them.

1.—"If there is one and the same parasite at work in all cases of carcinoma, how is it that the secondary growths in each variety so exactly (as a rule) imitate the character of their parent tumours? It seems necessary to suppose that actual fragments of the growth are carried away and develop on their own account."

There is no necessity to *suppose* anything of the kind. It is an undoubted and demonstrated *fact* that actual migration of malignant cells does occur; it is also a fact

¹ See "The Exogenesis of Cancer," *Quarterly Medical Journal*, May, 1903.

that the secondary growths *do not* imitate their parent tumours. These secondary growths are simply offshoots from the parent tumour which take on autonomous growth, exactly as a slip from a rose will do. The slip grows into a rose (not, for example, into a geranium), the same as its parent. It does not imitate it, it is actually and really a part of it. This actual migration of malignant cells is generally considered to be extraordinary and without parallel; but when the cause and structure of cancerous metastases are clearly understood, it becomes evident that this migration is not only not at all wonderful but that it would be extraordinary if such migration did not occur.

Moreover, it is not malignant cells only which migrate. It seems to be overlooked that normal cells also migrate. Without taking into account the leucocyte which finds its way everywhere, we know that bone-cells, for example, also migrate, as evidenced by the inter-fibrillar osseous deposit in muscle, called "*myositis ossificans*"—a term, by the way, not only absolutely non-descriptive, but also pathologically entirely erroneous.

With regard to malignant growths, there are two great classes, determined by their source of origin, viz., those derived from the epiblast and hypoblast, called *epitheliomata*, and those arising from the mesoblast, denominated *sarcomata*. In both classes the structure consists of cells and stroma, but the relationship of these to each other differs considerably.

In the *epitheliomata* the cells are derived from epithelium and lie more or less loosely in the stroma which consists of alveoli formed of connective tissue. The cells are not attached in any way to the alveoli or each

other, nor does connective tissue pass between individual cells.

Epithelial tumours are particularly rich in lymphatics. Lymph-channels communicate freely with the alveoli; in fact, the alveoli are really dilated lymph-spaces and form the radicles of the lymphatic trunks which lead to the lymphatic glands. Thus the epithelial cells are bathed in lymph, and being dislodged by the pressure of their own overgrowth, or in any other way, they must of necessity enter the lymph-stream. They are then carried by the current, and are arrested in the nearest lymph-glands.

Blood-vessels permeate the stroma and are often dilated. As they are penetrated by the actively proliferating cells, the latter enter the blood-stream also and are carried far away from the parent tumour.

In the *sarcomata* the arrangement is very different. The cells here are derived from connective tissue, and are embedded in the stroma which also passes between individual cells, and to it the cells are closely attached. There are no lymphatics in sarcomatous tumours, but the smaller blood-vessels are in direct contact with the cells, their walls being often formed of nothing but the cells of the sarcoma, a single layer of endothelial cells separating the blood itself from the cells of the tumour. Thus it is easy, and even inevitable, for the proliferating cells to enter the blood-stream and so be carried to distant parts.

This anatomical arrangement explains the fact that malignant epithelial cells so extensively infect the lymphatic glands and are more rarely conveyed by the blood; while the sarcomatous cells follow the course of

the blood-stream, leaving the lymphatic glands unaffected.

These living, infection-laden, autonomous cells, carried away by the lymph- and blood-streams as emboli, on becoming impacted, establish new malignant colonies by the active proliferation of the cells, and the action of the contained infective agent. These colonies, later on, repeat the process, until at length the organism is overwhelmed by their malignant action and the induced constitutional intoxication.

This propagation of cancer by metastasis shows how urgently imperative it is that, so long as removal by the surgeon is our only hope, extirpation of the growth should be carried out at the earliest possible moment before the local disease has had time to become more general and constitutional.

From the foregoing it must be evident that there can be no question of imitation or mimicry, and that genuine migration of the cells of the primary tumour does indeed take place, with formation of metastatic tumours, identical with the parent, as the result. The fact that cancer is spread in this way in the individual must simply be accepted. The fact that such extension is not analogous to the method of spread of infection in other diseases may be interesting, but it is otherwise of no moment. It would be absurd to suppose that pathogenesis can be fettered by analogy. One might with equal justice say that cancer cannot be a disease at all, because it is not analogous to any other known disease.

2.—A parasitic causation of cancer is improbable, because of the multitude of different growths.

There is, indeed a great variety of malignant tumours, but they have all the same clinical characteristics. They

all infect their environment, tend to ulcerate, extend by metastasis and ultimately destroy the organism.

Pathologically their variety depends solely and entirely upon the tissue of origin and their anatomical structure. As I have already said, there are two great classes of malignant growths, viz., those derived from epithelium and those arising from connective tissue, and all tumours conform in structure to one or other of these classes. The great variety of tumours is due to the great variety of the normal structures which arise from these two classes of tissue, and from which the tumours arise. The structure of these tumours is always the same—cells and stroma—and the variety in form and in consistence depends upon the relative proportion of these to each other, and their environment.

In soft tumours cells predominate, in hard stroma. There is no such entity as a specific cell indicative of cancer, every cell of a malignant growth being an infected cell derived from a normal structure. There is therefore no reason for supposing that a different infective parasite is necessary for each different variety of malignant growth. Electricity, for example, supplies the motive power to a great variety of machinery, but it is not therefore necessary to suppose that it assumes a different form according to the variety of machine driven by it.

3.—Distinction between benign and malignant tumours.

Clinically this distinction is exact, and such is freely admitted. Pathologically the distinction is not so clear, because the infective agent cannot be isolated and until this is effected pathologists must rely upon clinical indications.

The pathological distinction is undoubtedly interesting in the abstract, but, after all, it is the concrete, clinical distinction that concerns the unfortunate tumour-bearing individual. The pathologist asks, "Where does a benign fibroma cease and a sarcoma begin?" The clinician replies, "When the benign growth becomes infected from without, the benign tumour becomes malignant."

Benign growths being, for the most part, simple local hypertrophies of normal structures, are as liable to infection, after being rendered vulnerable by irritation, injury, or degeneration, &c., as are the tissues from which they spring, and even more so from the fact that their structure is often more hasty and ill-governed, and therefore more liable to external influences, than their parent tissues. No benign tumour forms a metastasis. When one is formed the tumour has ceased to be benign and has become malignant.

One of the most interesting and important points in cancer is the influence of age. Why should malignancy occur so generally in middle and later life? The reason is not far to seek. In early life repair is much in excess of decay, so much so that growth occurs. Later on decay and repair become evenly balanced, and growth ceases, but in middle and old age decay assumes the upper hand, and degeneration occurs; less resistance is offered by the tissues to external stimuli, and so vulnerability is established. Age is therefore a powerful factor in inducing the necessary condition precedent to cancer.

The opponent of the infectivity of cancer may very well say, "You reply to my objections, and no doubt consider that you have answered them satisfactorily, but what are the grounds for your own belief?"

Belief in infection is founded on clinical facts and logical proof. Pathological proof is certainly wanting, but that it will be eventually forthcoming is assured. It is only a question of time. This proof is, however, fortunately, not indispensable, for in many admittedly infectious diseases the infective agent is still only hypothetical.

No one can deny that cancer is most intensely infectious to the individual, and it cannot be gainsaid that all diseases which are infectious to the individual are capable of communication to others, and are also of external origin, therefore cancer is, and must be, of an infectious nature. Infection undoubtedly differs widely in degree, and fortunately cancer, like tubercle and leprosy, is of a low degree of infectivity, but all the same it is infective. The clinical facts are many and convincing—too many to be enumerated here.

The statistics of cancer-districts and houses, and the extraordinary testimony of Dr. Behla regarding the town of Luckau in Bavaria cannot be explained otherwise than by infection. Dr. Behla also supplies a number of cases of *cancer-à-deux*, of which I shall quote but one, viz., that of a man who presented himself at Tross's clinic suffering from malignant disease of the glans penis. On the removal of the growth and its microscopical examination it was found to consist of tissue identical in structure with uterine cervical epithelium, and it was further discovered that the man's wife was suffering from advanced cancer of the cervix uteri. This case alone is sufficient to prove that transference of cancer-cells occurred, that cancer is therefore contagious, and that it is of external origin. The long arm of coincidence cannot be successfully invoked here,

nor was this an isolated case, for over sixty such cases have been reported.

Then, again, cancer has been successfully transferred from man to man, and man to lower animals, experimentally, and although such successful experiments are not few in number, even one successful case is sufficient to prove the contagiousness of the disease.

Are we justified, therefore, in sitting still with folded hands and an "open mind" while this vile disease continues to increase by infection? Pending the universal admission of its infectivity should it not, at least provisionally, be considered infectious and action taken accordingly? Prophylaxis, by the thorough disinfection of all rooms and houses occupied by cases of cancer, and the complete destruction by fire of all dressings and dejecta (and such would be cleanly, if nothing else) could not fail to be productive of the greatest good.

It is hopeless to expect the adoption of notification, even voluntary, but medical officers of health might greatly help by instructing registrars to inform them at once of all deaths registered as due to malignant disease, and the co-operation of these medical officers of health with the practitioners signing the death-certificates would afford the best opportunity of thoroughly investigating each case.

What appears to me most deplorable is the utter indifference and supineness of the State with regard to the two great scourges of humanity. Tubercle has been proved to the entire satisfaction of all to be infectious, and yet the Local Government Board has not made the slightest effort to deal with tubercular disease in man¹

¹ Tubercle is now notifiable.

(it has in the lower animals!), not even suggesting notification; and it has been left to private enterprise to cope with the evil. So also with cancer.

The investigation of this disease is of national and imperial importance, but no help is forthcoming from the State. Money is lavishly squandered on the Army and Navy (*vide* the perpetual useless alteration in uniforms), and millions are freely wasted in war, but not one farthing has been offered to further the elucidation of the worst and most hopelessly fatal disease in existence. The only encouragement, even, which has been officially bestowed has been a friendly pat on the back from the Prime Minister, who recently offered his best wishes for success to the Cancer Research Committee.

In this country, science owes all its advance to the labours of private individuals, and with regard to the elucidation of cancer we shall have to trust to the co-operation of the clinician and the experimental pathologist.

THE INFECTIVITY OF CANCER.¹

MR. PRESIDENT AND GENTLEMEN,—The problem, “What is cancer?” is hoary with antiquity, yet, nevertheless, it is of perennial interest. On two previous occasions I have had the honour of addressing you upon this subject; once on its “Ætiology,” and again on its origin by “Exogenesis.” To-night I desire to direct your attention to certain points to which I have not previously referred, and to others already mentioned, but which I wish to enlarge upon and emphasize. That the importance of the problem is vital will be admitted by all, for, although many other diseases are just as incurable, and exact even a greater tale of victims than cancer does, there is no disease which is so universally dreaded, or causes more mental distress, in addition to physical suffering. This importance, moreover, becomes still greater when it is realized that the disease is becoming more and more widely diffused—that it is unquestionably increasing.

THE INCREASE OF CANCER.

An appeal to statistics leaves it in doubt whether the percentage ratio is or is not increasing, although the consensus of expert opinion is in favour of increase. No doubt the percentage ratio is affected by the greater accuracy in diagnosis and by the fact that the average

¹ An address delivered at a meeting of the East Yorks Division of the British Medical Association at Hull on November 15, 1907.

duration of life is markedly increased, but it must not be overlooked that many deaths have been certified as due to malignant disease which have not been confirmed by *sectio cadaveris*. Even, however, if the percentage ratio is not increasing, but remains stationary, it is still evident that cases of cancer must increase in number, *pari passu*, with the increase in population. When, therefore, the population of a given place doubles itself, as it does in x years (Vienna, e.g., has doubled itself in 25 years), then the number of cases of cancer must likewise, at the end of this period, be double what it was at the beginning.

Dr. S. Monckton Copeman states in the Guthrie lecture, delivered in 1907 at Westminster Hospital, presumably from reliable data, that of individuals at present living above the age of 35 years, 1 in 8 women and 1 in 12 men will eventually die from cancer. This means that cancer will decimate those of an age above 35 years—truly an appalling prospect!

I regret that I am able to corroborate this estimate of Dr. Copeman from statistics supplied by my own practice. During the last 19 years there have been 1,256 deaths certified, of which 136 have been due to cancer (51 males and 85 females), and this yields an annual average of 10.82 per cent. of deaths due to malignant disease. The actual figures are given on the following page:—

CANCER HYPOTHESES.

Since the *causa causans* of cancer has not yet been demonstrated, it is not remarkable that many causes should have been suggested and many hypotheses propounded. Indeed, such causes and hypotheses are

Year	Total deaths			Due to cancer			Percentage
1903	...	66	...	5	(4 female, 1 male)	...	7.50
1904	...	78	...	11	(6 " 5 ")	...	14.10
1905	...	99	...	8	(5 " 3 ")	...	8.00
1906	...	72	...	7	(6 " 1 ")	...	9.70
1907	...	74	...	13	(6 " 7 ")	...	17.56
1908	...	70	...	11	(7 " 4 ")	...	15.71
1909	...	49	...	3	(3 " —)	...	6.12
1910	...	64	...	1	(— " 1 ")	...	1.56
1911	...	52	...	5	(1 " 4 ")	...	9.61
1912	...	52	...	5	(5 " —)	...	9.61
1913	...	71	...	6	(4 " 2 ")	...	8.45
1914	...	65	...	10	(7 " 3 ")	...	15.38
1915	...	66	...	8	(7 " 1 ")	...	12.12
1916	...	50	...	6	(3 " 3 ")	...	12.00
1917	...	60	...	6	(3 " 3 ")	...	10.00
1918	...	81	...	11	(5 " 6 ")	...	13.58
1919	...	72	...	7	(4 " 3 ")	...	9.72
1920	...	61	...	3	(1 " 2 ")	...	4.91
1921	...	54	...	10	(8 " 2 ")	...	18.51
19	1,256			136	(85 female, 51 male)		Av. 10.82
Age							
	30—40	8		
	40—50	13		
	50—60	21		
	60—70	44		
	70—80	37		
	80—90	12		
	94	1		
136							

NOTE.—At the time that this Address was delivered statistics were given from 1903 to 1907 only, but these have here been augmented by the addition of results up to the end of 1921.

countless, and while their attempted recapitulation would doubtless be of great interest, such would be but vain iteration. Suffice it to say that all these alleged causes and suggested hypotheses crystallize out into two classes: (1) *intrinsic*, of which the number is "legion"; and (2) *extrinsic*, of which there is but one. *Auto-genesis* or *Exogenesis*? "that is the question." No doubt the calm, philosophic, and scientific attitude to maintain upon a subject which cannot be proved to

demonstration is that of "the open mind"; but even the calmest, unless he is a disinterested Gallio, must find it hard to remain in a state of passive imperturbability when so much is at stake. Hence it is that there are warm advocates of both these views. The exponents of exogenesis believe that the evidence in favour of the extrinsic origin of cancer is overwhelming, and that this hypothesis will satisfactorily account for the incidence of cancer in every case, and they acknowledge only one possible cause—viz., parasitism. The believers in auto-genesis, on the other hand, chiefly maintain a negative attitude, denying the possibility of an extrinsic cause, but fail to formulate any practicable hypothesis which will explain the origin of the disease in every case. They suggest theory after theory, continually shifting their ground, and nohow can they suggest satisfactorily why cancer should arise, apparently *de novo*, in any single case.

Again, the supporters of exogenesis hold that if cancer has an intrinsic origin—e.g., "running to seed"—it would not only be very much more prevalent than it is, but that few, if any, could escape from it. They also hold that an extrinsic origin would satisfactorily account for the proportion of individuals attacked, and believe that the widespread occurrence of the disease among vertebrates indicates the omnipresence of a specific parasite, and that those who are attacked are simply those whose vulnerability, from whatever cause, has permitted its access to the host and favoured its development. The opponents of exogenesis urge that the extrinsic origin of cancer is impossible because it is not entirely analogous to any known infectious disease. The reply to this is that it is most unreasonable and illogical

to presume that pathological processes can be in any way limited or even influenced by analogy ; and, furthermore, that analogy is quite incapable of proving anything. At the most, analogy can suggest mere probability, and is, after all, only a very convenient method of comparison between processes which resemble one another.

The following may be cited as a concrete example of the futility of trusting to analogy to establish a conclusion. When Farmer, Moore and Walker announced their interesting discovery that the karyokinesis of the cells forming a malignant neoplasm is heterotype in character, and that the karyokinesis of the cells of normal reproductive tissue is also heterotype, it was actually stated that " malignant new growths were virtually reproductive tissue arising in abnormal situations " !

Now, which hypothesis is most probably right—autogenesis or exogenesis ? It is difficult, and even impracticable, to discuss the former, since the various intrinsic hypotheses are too numerous and too elusive, while their very multiplicity testifies to their inadequacy, but exogenesis, having only one string to its bow—viz., parasitism—can be considered. If further information regarding these numerous intrinsic hypotheses and suggested causes of cancer is desired, I would refer you to a work recently written by Dr. Jacob Wolff of Jena, entitled " Die Lehre von der Krebskrankheit von den aeltesten Zeiten bis Gegenwart " (" The History of Cancer from Ancient Times to the Present "). It was published in 1907 by Gustav Fischer and consists of 747 octavo pages.

Since cancer is admittedly a specific disease which

runs a definite course of attack, extension by dissemination similar to that of many other diseases, such as tubercle, syphilis, malignant endocarditis, &c., constitutional intoxication, and ending only in death, believers in exogenesis cannot admit the possibility of any somatic cell spontaneously developing specific malevolent action. They are constrained to believe that a specific disease can no more originate without the presence of a specific morbid agent than that parthenogenesis can occur in the vertebrata. This specific agent, they consider, cannot be other than an extrinsic parasite, either a microphyte or a microzoön.

PARASITISM.

It may truly be said of parasitism what Shakespeare says of Cleopatra, by the mouth of Enobarbus. "Age cannot wither her, nor custom stale her infinite variety." The universality of parasitism is quaintly but concisely expressed in the quotation from Professor Russell Lowell :—

"Great fleas have little fleas
Upon their backs to bite 'em ;
And little fleas have lesser fleas,
And so *ad infinitum*."

What is true of the *pulex irritans* is equally true of all creation. The diseases which we already know to be caused by parasites are very numerous, and so many more are becoming suspected of a like origin that presently one will be driven to conclude that all the ills to which flesh is heir, excepting accidents, are due to parasitism. Organic chemistry has been defined as "The continued history of carbon." It appears that we shall soon be justified in defining all disease (apart

from accidents) as "The continued history of parasitism."

IS CANCER INFECTIOUS?

If cancer is caused by a parasite it comes under the designation of "infectious." *Is cancer infectious?* Before answering this question, which is the theme of this essay, it were well to define what I mean by the terms "infection" and "infectivity." "Infection" is a comprehensive term and may be defined as the transmission of a disease from one individual to another, directly or indirectly, by the agency of a specific micro-organism, either a bacterium or a protozoön. *I believe cancer to be thus transmissible.* Infection varies greatly in degree, and cancer is evidently not infectious to the same extent as many other diseases—e.g., variola. It is probably acquired much as enterica is by introduction through the mouth; or as syphilis is, by contact; or as tetanus is, by access of the germ to any vulnerable part; or it may be through the agency of an intermediate host, as is the case in malaria or trypanosomiasis.

It has long been maintained, and many concrete instances have been quoted to prove, that cancer is transmissible by direct contact, as in "cancer-à-deux," of which "coition-cancer" is an example. Such transmission, however, has been generally denied and accounted for by fortuitous coincidence; but as transmission by implantation from one lower animal to another of the same species has been successful, and freely admitted to be so by all, the transmission in the case of "cancer-à-deux" has had reluctantly to be admitted as at least possible. This transmission has been designated "transplantation" and not admitted to

be the successful and genuine inoculation of a specific disease. Now, if the "transplanted" cancerous tissue resembled a skin graft, always remaining local and forming no tumour, or if it merely continued to grow locally by proliferation without the usual metastatic dissemination and constitutional intoxication, and never caused death, then the term "transplantation" might be justified; but when the characteristic evolution of malignant disease follows, terminating the life of the invaded host, one can only regard the case as one of genuine inoculation of a specific disease by a specific agent—i.e., that it is the result of true "infection."

In connexion with the successful inoculation of cancer in the lower animals of the same species, and also as bearing on the question of "cancer houses and rooms," an interesting communication was made by Dr. Gaylord of Buffalo entitled, "Evidences that Infected Cages are the Source of Spontaneous Cancer developing among small Caged Animals." I regret that the time at my disposal is too short to permit of reference to this paper at length, but I am sure you will find it well worthy of perusal. Dr. Gaylord first refers to the endemic occurrence of cancer of the thyroid in brook trout hatcheries in Germany, recorded by Pick. Pick states that his investigations show that certain hatcheries are entirely free from this affection and that where the fish are affected the disease is confined to individual tanks or pools in which the fish are kept; that wild fish introduced into those ponds to replenish the stock acquire the disease, and this, to his mind, eliminates heredity as a factor in the development of the disease. The nature of the affection is true carcinoma, and he concludes that this endemic occurrence of cancer among

trout in certain tanks only indicates that the water of these tanks contains the agent which is the cause of the disease. Dr. Gaylord then proceeds to narrate many instances of cancer occurring in rats which developed the disease after occupation of cages previously occupied by other rats suffering from cancer. These instances are quoted by several observers, both medical and lay, in the latter case by the man who supplied rats to the laboratory for experimental purposes. It was found that when the infected cages were thoroughly disinfected no further infection occurred.

AUTO-INOCULATION OF CANCER.

To my mind, the strongest argument which can be adduced in favour of the exogenesis of cancer is one of its most distinguishing characteristics—viz., its undeviating method of growth and dissemination by proliferation and metastasis and auto-inoculation. Although cancer is unquestionably purely local at the outset, unfortunately it does not long remain so. Indeed, it would be completely under the control of the surgeon's knife and would lose all its terrors were it not for the fatal metastases which are invariably formed and that with a startling rapidity which is not sufficiently realised.

Mr. C. B. Lockwood has drawn attention to this rapid extension of the disease in a communication entitled, "Carcinoma of the Breast and its Spread into the Lymphatics." He points out that in malignant growths of organs which have no capsule—e.g., the mamma, tongue, or pharynx—hardly any interval of time exists between the onset of the disease and its spread into the lymphatics. He says, "In the smallest

carcinoma of the breast that I have seen the neighbouring lymphatics were already cancerous." It is this inevitable and rapid metastasis which is responsible for the equally inevitable failure of the great majority of operations for the removal of malignant neoplasms.

Mr. H. T. Butlin, in his recent address in surgery at the annual meeting of the British Medical Association in 1907, on "The Contagion of Cancer in Human Beings and Auto-inoculation," says: "The key to the problem of communicability of cancer in human beings must surely lie in the study of auto-inoculation. If auto-inoculation can be proved on such evidence as would be admitted in a court of law there is a *primâ facie* case for contagion." He then goes on to say: "If the proof of auto-inoculation falls through from the lack of sufficient evidence it is no longer worth while to pursue the study of contagion from individual to individual." Granted, but auto-inoculation of cancer requires no proof. Unfortunately for mankind it is indisputable; it is a marked and only too self-evident characteristic feature of the malady. Every metastasis is a true auto-inoculation. So, also, is every so-called "recurrence." There is obviously no such process as recurrence. That which has been removed cannot recur, but what has been *left behind* continues to grow. Worse still, what has been set free from divided lymphatics and the tumour itself by the surgeon's knife, and what that infected knife has itself inoculated in and about the wound infallibly grows also. Mr. Butlin's conception of "auto-inoculation" appears to be a very limited one, applying only to the inoculation of an adjacent healthy surface by an affected one. Although it is well known that this auto-inoculation of adjacent

structures not infrequently happens, its absence or presence is merely of academic interest. Its presence is confirmatory, but its absence cannot in the slightest degree invalidate the obvious fact that auto-inoculation is one of the most marked characteristics of cancer. Mr. Butlin's "key" is therefore ready to his hand, for the condition he considers necessary to establish a *primâ facie* case for contagion is, only too clearly, already in evidence.

Mr. Butlin further says: "Experiment has proved that successfully implanted carcinoma invariably presents, both in the graft and its metastases, the characters of the carcinoma from which it was implanted"; also that, "no transformation has yet been observed of one variety into another variety." Then, as a corollary to this, he adds, "all cases of reputed contagion of cancer, in which the disease is not of the same variety, must be unhesitatingly rejected." With regard to his first point, that grafts and their metastases always present the same characters as the parent carcinoma, it could not possibly be otherwise. It is another characteristic of cancer that it "breeds true," and every metastasis, wherever situated, is an actual fragment, or graft, of the original neoplasm, and a cancerous graft implanted successfully in another individual is, to all intents and purposes, a metastasis of the tumour supplying the graft. Consequently, all implanted carcinoma grafts and their metastases must be of the same variety as the original growth. As regards the second point, Mr. Butlin must be unaware of the recent experiments of Ehrlich and Apolant, which have demonstrated beyond doubt that even a carcinoma can, under given conditions, lead to the development of a sarcoma in con-

nective tissue immediately adjacent to it. If, then, a carcinoma can give origin to a sarcoma, it is obviously even more probable for one variety of carcinoma to originate another variety of carcinoma. It does not, therefore, appear necessary, after all, to reject the cases of reputed contagion in which the disease is not of the same variety. Farther on I shall endeavour to show that any one variety of malignant neoplasm may originate any other variety. The reason for Mr. Butlin's rejection of these cases is entirely consistent with his belief, which is that, although he considers cancer to be a parasitic disease, he is not apparently able to admit the logical sequitur that a specific parasitic disease must be necessarily caused by a specific extrinsic parasite. In the Bradshaw lecture delivered by him in 1905 Mr. Butlin maintains that "cancer is a parasitic disease," but that the "carcinoma cell" itself is the parasite and "acts as an independent organism like many a protozoön."

IS THE CANCER CELL ITSELF THE PARASITE?

Imprimis, there is no such entity as a special "carcinoma cell." Professor D. J. Hamilton, of the University of Aberdeen, says, with reference to carcinomata: "The old notion that there was a special cell indicative of cancer is erroneous. The only point which is typical about the cells of the tumour is that they are always epithelial; they have no constant morphological features beyond this." The elements of any malignant neoplasm are simply ordinary somatic cells which have undergone abnormal, exuberant proliferation under a specific stimulus. Transmitted by the lymphatics and blood-vessels, or implanted deliberately by artificial

means, these cells certainly *appear* to act like independent parasites, but they act in this manner not voluntarily but only by virtue of the intracellular malignant stimulus which is clearly the micro-parasite.

It is impossible for the " carcinoma cell " to be the true parasite.

Let it be supposed for a moment that the " carcinoma cell " could be the parasite, then—1. There must have been an original neoplasm for it to come from. How, then, did this original growth arise? Certainly not from any pre-existing " carcinoma cell," since "*ex nihilo nihil fit.*" 2. All cases of cancer would also of necessity be due to direct contact. 3. All cases of cancer would be of only one variety—viz., the same variety as the original neoplasm from which the " carcinoma cell " emanated. Now, we know that comparatively few cases of cancer are due to direct contact; so few, indeed, that they are not generally accepted as genuine, and the " cell parasite " would account for them only. The great majority of malignant neoplasms arise apparently spontaneously and sporadically; also it is a characteristic of cancer that its variety is very great. It is obvious that the origin of cancer and its great variety must be explained in some other way than by the direct implantation of a " carcinoma cell " or by the preposterous suggestion that any somatic cell by any intrinsic stimulus can possibly develop *de novo* a specific disease such as cancer. We may as well be asked to believe that tuberculosis, for example, can be originated by the agency of an intrinsic stimulus. I beg to submit that the living implanted cell which may be the starting point of any malignant neoplasm must have been derived from a pre-existing neoplasm, and that its malign-

nant influence is due to an intracellular micro-parasite endowed with extraordinary and most malevolent powers. It is this intracellular entity which is the "*deus ex machinâ*," or, as it might be more appropriately designated, the "*diabolus ex machinâ*," of Mr. Butlin's "carcinoma-cell parasite," and this micro-parasite can, and does, exist independently of any cell. It alone is responsible for the original of all neoplasmata.

With regard to his "carcinoma cell," Mr. Butlin states that it exhibits a singular tenacity of life, for such cells have been kept for many days at a temperature below 27° F. or have been placed in sterilized glass flasks and sent across the sea by post and yet have in each case been inoculated with as good a result as if they had just been transplanted from one individual to another. Later, however, he adds that all experiments made with the object of cultivating the "carcinoma cell" outside the body of the host have resulted in failure, and that Ballance and Shattock have reported that they have been unsuccessful even in keeping these cells alive outside the host. These statements are contradictory. It is impossible for living cells of any kind, malignant or otherwise, to retain their vitality for any length of time after removal from their natural environment. Everyone knows that any cells can, by sterilization, be preserved from decomposition for an indefinite time, but this preservation is not synonymous with vitality. How, then, can these conflicting statements be reconciled, and how was it that these dislocated "carcinoma cells" were successful in inoculating fresh hosts as alleged? Their success was clearly due to the vitality of the intracellular parasite itself and not of the encap-

suling cells. The vitality of the intracellular parasite is of paramount importance for the perpetuation of its species and is very great, whereas the vitality of the dislocated "carcinoma cells" is of very brief duration and of only secondary importance. Although the cell itself is dead it can still originate a neoplasm by virtue of the living intracellular parasite, but the resulting neoplasm is, as I shall presently show, of a different type from that originated by a living cell.

CLASSIFICATION OF NEOPLASMATA.

All neoplasms may be divided, clinically, into: (1) *benign*; and (2) *malignant*.

The *benign* are, for the most part, simply local hypertrophies of normal tissue and remain so unless they become infected like any other normal tissue, in favourable circumstances, and they do not form metastases. These benign tumours do not require any specific stimulus to originate them, simple stimulus of a mechanical nature being quite sufficient in many cases for the purpose. They are comparable to the pearl of an oyster which is simply the deposit of a normal substance around a foreign body.

Malignant neoplasms are divided into: (1) *epitheliomata*; and (2) *sarcomata*. *Epitheliomata* arise from epithelium, originally derived from the epiblast and hypoblast. They disseminate themselves chiefly by the lymphatics, but also, to some extent, by the blood-vessels. *Sarcomata* arise from connective tissue, originally derived from the mesoblast. They, on the other hand, chiefly utilize the blood-vessels for propagation but they also utilize the lymphatics. Malignant neoplasms cannot arise without the agency of a definite

specific stimulus. These two great classes are further subdivided into very many varieties as regards structure, but in all other essentials they are practically the same in each case. This great variety is, simply and entirely, due to the anatomical diversity of the tissues in which they occur and their environment. As Professor Hamilton points out, all such subdivisions as osteoid, villous, colloid, chondroid, encephaloid, &c., are "useless and misleading."

With regard to their method of origin in the tissues, malignant neoplasms are of two distinct types: (1) primary; and (2) secondary. The primary are those formed by the proliferation of the cells of the *local* tissue invaded by the parasite itself. When the parasite is in a *free* state or encapsuled in a *dead* cell thrown off from the surface of a neoplasm (which practically amounts to the same thing, for a cell devoid of vitality is obviously incapable of proliferating and so originating a tumour composed of its own elements), and when it gains access to the host, then the resulting neoplasm will consist of the proliferated elements of the *local* tissue cells *invaded*. Thus the free parasite emanating from a glandular-celled carcinoma may originate a squamous-celled carcinoma in another individual if it invades such tissue, or the free parasite from a squamous-celled carcinoma—of, e.g., the tongue—may give rise to a columnar-cell carcinoma of the stomach or rectum, or to a spheroidal-celled carcinoma of the mamma, or to any other variety of carcinoma, according to the structure of the tissue invaded. The great majority of malignant neoplasms which arise, apparently *de novo*, are of this primary type. They are originated directly by the parasite itself and indirectly by the tumour from which the parasite is

set free. Thus the great variety of cancer is accounted for and to the free parasite are we indebted for the original neoplasm.

The secondary are formed of *alien* cells by the proliferation of the directly implanted infective tissue cells themselves, acting under the stimulus of intracellular malignant influence, the micro-parasite. When the parasite is encapsuled in a *living* cell and this cell gains access to any host the resulting neoplasm will be of the same variety as the *invading cell*, being formed by its proliferation in its new situation and not by the proliferation of the cells of the local tissue invaded, as in the primary type. All that the *invaded* tissue cells do is to provide ordinary nutriment for the proliferating *invading* cells. Thus, the parasite-bearing *living* cell from, e.g., a columnar-celled carcinoma will originate another columnar-celled neoplasm by its own proliferation, quite irrespective of the structure or situation of the tissue invaded. Such infection is immediate and direct as regards the implanted cell and indirect as regards the inclosed parasite. All metastatic growths and all auto-inoculations are of this secondary type. For example, the metastasis from a neoplasm of the rectum established in the liver or lungs consists of proliferated rectal epithelial cells. All cases of "cancer-à-deux" and all cases of deliberately implanted cancerous growths are also of this type. So great are the activity and vitality of these malignant parasite-bearing cells that even one such left behind after an operation for the removal of a malignant neoplasm is able to reproduce it. Thus, the infection of invaded tissues by a parasite-bearing living cell, with subsequent proliferation of the latter, corresponds to what occurs after an unsuccessful

operation. Now we see that Mr. Butlin's "carcinoma cell" parasite could only originate this secondary type of neoplasm while the origin of the enormous majority of malignant new growths is left unaccounted for by his hypothesis; but the primary type of origin accounts for this majority and supplies the original neoplasm from which the living cell, apparently acting as an independent parasite, emanates. It also accounts for the great variety of malignant neoplasms, a variety only limited by the anatomical diversity of tissues.

All this demonstrates how *true* a parasite the micro-organism responsible for cancer is. In the secondary type we find it comfortably ensconced in a living cell which it compels to slave for it, when implanted in any situation, stimulating it to proliferate and so provide accommodation for its numerous progeny. It exerts no personal influence whatever on the surrounding local tissue cells, which are generous enough to furnish the invaders with food supplies. It is only when death of the host occurs, or if perchance a cell dies and becomes detached from the colony, that its tyranny ceases for a time. Now it must make personal exertion and endeavour to find a fresh victim in the cell of the nearest available living tissue. Having succeeded in gaining a footing it proceeds to induce the selected invaded cell to commence work by proliferating, and the process progresses as before except that this time it is the cells of the local tissue which have both to increase in number and find their own food. This is the primary type.

In all other parasitic diseases the micro-organism of causation remains free and active personally, but the cancer parasite is the *truest* parasite of them all, for it never exists free if it can avoid it, but clings to its cell-host with indomitable pertinacity.

THE PARASITE OF CANCER.

Although its presence is proved by induction, as is also the existence of, for example, the micro-parasite of variola, the parasitic agent of cancer is, as the Germans say, "*noch nicht konstatiert*" (it has not yet been conclusively demonstrated). Doyen of Paris believes that the bacterium known as "*micrococcus neoformans*" is the germ responsible for cancer. This belief appears to be corroborated by the researches of Dr. C. Jacobs and Dr. Victor Geets, the result of which was communicated by them to the Royal Belgian Academy of Medicine at Brussels in January, 1906. These observers report that it is practicable to immunize the human organism by means of a series of inoculations of the *micrococcus neoformans* vaccine, provided that these are properly controlled by examination of the opsonic power of the blood. They cultivated the micro-organism from 90 per cent. of tumours examined and succeeded in producing localized, or generalized, neoplastic lesions in 30 per cent. of the cases, by inoculating young and vigorous cultures of the micro-organism into mice and white rats. They prepare the vaccine in exactly the same manner as Koch prepares his tuberculin T.R. and treat their patients in a similar way to the vaccine treatment of tuberculosis. They allege that in some cases they obtain cures, but point out, however, that as tuberculin does not cure all cases of tuberculosis, cancer vaccine, too, cannot cure all cases of cancer. Success or failure depends entirely upon the reserve of vital energy and capacity for reaction which each patient possesses, and these differ in each case. Other observers—e.g., Wright—have failed to confirm these results, and they are, I believe, now discredited.

Roswell Park, Gaylord, and others in America believe that cancer is caused by an organism of the same nature as the plasmodiophora brassicæ. Their observations seem to prove that minute plasmodiophoræ are present in carcinomatous tumours and that they can be grown from such tumours through a definite stage in their life cycle. In summarizing their results and conclusions Dr. W. Ford Robertson and Mr. Henry Wade state that they had been able to recognize in carcinomatous tumours bodies which, in their form and in their reaction to the platinum and silver-gold methods, are identical with the plasmodiophora brassicæ but from one-tenth to one-twentieth of the size. They had succeeded in growing from three carcinomata an organism which accurately represented the post-spore or pre-amœboid stage of a plasmodiophora. If plasmodiophoræ were present in carcinomatous tumours it was hardly open to doubt that they had the same relation to the morbid growth as the plasmodiophora brassicæ had to "club-root," that was to say, that they were the determining ætiological factor.

In a later communication (August, 1907) Dr. Ford Robertson claims that he has obtained much new evidence which he considers confirmatory of this view, evidence derived from cultural and histological observations of the occurrence of special intranuclear bodies of the nature of those previously described, to show that structures morphologically identical with the spirochæta microgyrata can be demonstrated in human carcinomata. Gaylord and Calkins have also described a special spirochæta in primary and transplanted carcinoma of the breast in mice. The confirmed discovery that spirochæta pallida is the ætio-

logical factor in syphilis is analogically suggestive of a spirochætan cause of cancer. Much undoubtedly remains to be done, however, before the elusive parasite can be demonstrated to the satisfaction of all; but these discoveries tend to show that the net is gradually, but surely, closing around it.

I offer the suggestion that the examination of fresh, living, carcinoma cells on the warm stage of the microscope would result in much additional and valuable information; also that the employment of high power microscopy would be a great aid to investigation. The objective of a microscope reaches the limit of its useful development in the direction of increasing magnifying power as soon as, by reason of the shortening of the focal length, the diameter of the object glass, in its principal plane, is reduced to something not much less than the diameter of the pupil. Added power, however, to any required extent can be obtained by high power oculars, but the image thus obtained is rendered defective by the blurring of the image from dust and obstructions in and on the lenses, and by the observer's eyelashes, tears, and *muscæ volitantes*; but, quite recently, the image has been rendered perfectly clear and very high magnifying power obtained by the skill and ingenuity of an expert in microscopy. In February, 1905, at a meeting of the Royal Institution of Great Britain, Mr. John W. Gordon described a device by which a magnification of 7,000 diameters could be obtained as well as a perfectly clear field of view. Mr. Gordon substitutes for the eyepiece a compound microscope with a half-inch objective and an ocular magnifying eight times. A ground-glass screen is held in the image plane of the principal microscope,

and this screen is made to revolve and also at the same time to oscillate eccentrically. The screen abolishes the intrinsic images of dust and foreign matter and the eccentric rotary motion renders the screen invisible.

Quite as important as high magnification of the image is good field illumination. Dr. Siedentopf has devised a system of dark field illumination, applicable to objectives of the widest possible aperture, which renders visible objects so minute and clustered so close to one another that by no other known contrivance can they be rendered separably visible at all. I must not further occupy time in describing this system of illumination and would refer those interested to the *Proceedings of the Royal Institution of Great Britain*, Vol. XVIII.

There is another desideratum of the greatest importance in the histological investigation of cancer which, I fear, is more likely to be sought for than found, and that is a specific staining reagent which will act on cancerous tissue in an analogous manner to the selective action of iodine upon the diseased areas in amyloid disease which renders them clearly distinct even to the naked eye. It is true that there is such a selective stain, but it acts only in one species of malignant neoplasm. I allude to the staining by melanin in melanotic cancer. Its presence makes it possible not only to detect every particle of original and metastatic growth in this variety, both macroscopically and microscopically, but it also permits optical demonstration of the method of dissemination by the blood-vessels and lymphatics. This has been most ably demonstrated by Mr. W. Sampson Handley in his Hunterian lecture on the Pathology of Melanotic Growths in Relation to their Operative Treatment.

THE CONDITION PRECEDENT.

Since perfectly healthy tissues are probably immune from, or invulnerable to, the attack of the cancer parasite, there must be causes predisposing to the acquisition of the disease, and these go to form what I have called the "condition precedent." This condition is induced by whatever lowers or impairs the power of resistance of the body to infection. In the case of cancer the chief factor in producing this vulnerability is degeneration of tissue from any cause, but more especially that due to obsolescence of organs, senescence, and senility, for cancer is, *par excellence*, the disease of advanced age, though by no means confined to it. This is obviously due to the fact that in those of middle and advanced age decay is in marked and increasing excess over repair (the reverse being the case in youth), and the tissues are less equal to the strain of resisting the attack of the aggressive parasite, especially when this degeneration exists in conjunction with the other predisposing factors of this condition, which are chronic disease, continued irritation, traumatism, and congenital susceptibility. In my opinion, it is the failure to realize the invulnerability of young and healthy subjects which is one of the causes of so many unsuccessful inoculation experiments. I have discussed this point fully in another paper.

CHANNELS AND MODE OF INFECTION.

I have elsewhere fully considered the channels of infection and it remains to consider how one becomes exposed, unknowingly, to the risk of attack by the parasite. This evil agent appears to be practically

omnipresent, as so many other pathogenic micro-organisms are, such as the bacillus tuberculosis, the bacillus tetani, and the malevolent legion of micrococci, and it is ever ready to act aggressively as opportunity arises and circumstances favour. One hardly appreciates how very close the relationship is, if only indirectly, with our neighbours, including those suffering from cancer. All our food, both cooked and uncooked, passes through the hands of many individuals, and the only safeguard, cleanliness, on their part is practically beyond our control. As evidence of this I give you an instance from personal experience. A widespread epidemic of enteric fever which occurred in a village near Driffeld, in which I had several patients, was easily traced to an imported case which was nursed by a woman who supplied milk to all those attacked. This woman, though altruistic, was a most uncleanly person and made it her practice to milk her cows without even washing her hands, and that immediately after attending to the discharges and soiled linen of her patient. Much vegetable food, e.g., salads and fruit, is eaten uncooked. Each strawberry, for example, we eat is gathered by the unwashed hands of the gatherer. Strawberries also lie very near the ground, as do lettuces, &c., and are readily accessible to domestic animals, such as the dog and cat, which also suffer from external cancer as well as from intestinal worms. There is an article published in *The Lancet* of July 16th, 1904, entitled "Fruit and Filth," which will well repay anyone's perusal, provided the reader is not too greatly under the dominance of his nerves, or has not too lively an imagination, for anyone who reads that article is not likely to touch strawberries again unless he picks them himself from plants above suspicion of defilement.

Far be from me the desire to harrow your feelings too deeply, but how, let me ask, is one to know that the common house-fly, which crawls all over our bread and butter, or other article of food, was not, immediately before, disporting itself on the surface of a cancerous wound? Flies are well known to carry tubercle and typhoid bacilli, as well as other pathogenic micro-organisms, on their feet, and in the stomach, and it is also well known that they have infected food and drink with these germs, with disastrous results. I would refer you to a very able and suggestive communication published in *The Lancet* of July 27th, 1907, under the title of "The Carriage of Infection by Flies." This article gives the result of experiments made by Dr. R. M. Buchanan, bacteriologist to the corporation of Glasgow, with the object of demonstrating this fact. I wrote to Dr. Buchanan to inquire if he had made any experiments as to the cancerous contamination of food by flies and received the following reply: "I have not yet tried the experiment you suggest with reference to cancer, but hope to do so as soon as I can obtain material. The same problem presented itself to me in connexion with the death of a friend some years ago from intestinal cancer."

One's own footgear must bring much dust, laden with all kinds of pathogenic micro-organisms and, on occasion, dust from a cancer sufferer's room, into one's house, and it may easily find its way to one's food, &c. In this connexion the Eastern custom of leaving the outside shoes at the entrance of the house has, truly, much to commend it. Another risk to which we are exposed is eating the flesh of animals which have been suffering from malignant disease when killed. In

December, 1904, according to press cuttings in my possession, a man was fined £50 and £7 costs at the Guildhall, London, for sending meat to Smithfield which on examination was found to be sarcomatous. It cannot be assumed that this is a solitary instance, only it happened to be discovered. Cooking is said to minimize risk, but underdone meat is not unpopular.

I once knew a dentist who suffered from cancer of the prostate, from which he eventually died, and who followed his occupation during his illness. One of the physical signs of his malady was a urethral discharge, which necessitated frequent manual attention. I have no reason to doubt that he occasionally washed his hands! In my own practice a patient suffering from a fungating cancer of the mamma was nursed by a woman who frequently had occasion to remove soiled dressings and who was not particularly cleanly in her habits, and did not always wash her hands before meals. Within a year of her patient's death the nurse developed cancer of the stomach and died. This may have been a coincidence, but I believe it to have been a case of indirect infection, a neoplastic disease of the primary type.

I have thus indicated a few possibilities; some may be considered far-fetched, still they are possibilities, and unpleasant ones; doubtless many more will occur to yourselves.

PROPHYLAXIS.

From the foregoing it is obvious that the only reliable prophylactic against cancer as well as other filth diseases, and it is an efficient one, is cleanliness in its widest sense. Earth burial, with all its hideous possibilities, should be superseded by cremation of all who

die from infectious disease, and especially from cancer. Cremation would deal with the disease at its source. All soiled dressings and discharges from cancerous subjects should be destroyed by fire and all rooms inhabited by them should be most thoroughly disinfected both during the illness and after death. No food should be prepared or consumed with unwashed hands.

NEW FACTS ABOUT CANCER.

Within recent years several new facts have been discovered about cancer. 1.—The mitosis of the cells of malignant neoplasms has been found to be heterotype in character, whereas the mitosis of all somatic cells with one exception, and of the cells of benign tumours, is homotype. The mitosis of normal reproductive tissue is also heterotype. 2.—It has been discovered that cancer is not restricted to the higher vertebrata, e.g., man and the domesticated animals, as was at one time supposed, but that it occurs in all vertebrata, with the possible exception of certain reptilia. The malignant growths occurring in other vertebrata are identical with those found in man, clinically, pathologically, anatomically, and microscopically. 3.—The transmissibility of malignant new growths from one lower animal to another of the same species has been demonstrated.

With regard to the first of those discoveries it was the resemblance between the mitosis of malignant cells and that of normal reproductive tissue cells which led to the enunciation of the famous analogical fallacy that malignant new growths are merely reproductive tissue in abnormal situations. The heterotype character of the mitosis of malignant cells and the homotype character of somatic and benign tumour cells are, indeed, of

academic interest, but of little or no practical importance beyond affording a possible means of differential diagnosis in some doubtful cases which, however, would signally fail in the case of tumours of the reproductive tissues, since the mitosis is heterotype in either case, whether benign or malignant. It has been suggested to me that the fact of the mitosis of malignant and generative tissue cells being heterotype in both cases was important as showing that generative tissue cells, like those of cancer, have the power of proliferation. Of course, this fact cannot prove any such power, since analogy can prove nothing, but can merely suggest; still, if it could prove it it would not be necessary to corroborate the power of proliferation of generative cells, since the first infant one comes across is ample and convincing proof of that! At the same time there is a very suggestive parallel between the two proliferations. *Neither generative tissue nor other normal tissue cells can proliferate without a specific stimulus.* In the case of generative tissue the ovum only commences to proliferate when it has been invaded by the spermatozoön, which acts practically as an extrinsic specific protozoan parasite. The proliferation is enormous and rapid. The resulting tumour is benign, though some might consider it to be a malignant tumour in a normal situation! It is easily got rid of, and "recurrence" does not take place unless there is reinfection! In the case of somatic cells proliferation only commences when they are attacked by the cancer parasite. Mitosis becomes heterotype, proliferation goes on apace, and the tumour is malignant and impossible to eradicate. Nothing is known of the method of the influence of the cancer parasite on the somatic cell, any more than the influence of the sper-

matozoön on the ovum is understood, but it will be admitted that the one process is equally as marvellous as the other.

With regard to the second of these facts, among the vertebrata in which cancer has been discovered to exist are certain fishes, found both in rivers and in the ocean round our coasts. This fact has induced the director of the Imperial Cancer Research Fund to state that "the wide zoological distribution of malignant new growths indicates that the cause of cancer is to be sought in a disturbance of those phenomena of reproduction and cell-life which are common to the forms in which it occurs." Thus he makes a statement of opinion which clearly indicates how little is the help towards solution that may be expected from intrinsic hypotheses and their advocates. To the "man with the open mind," however, it might probably occur, as it certainly does to me, that this wide distribution of cancer throughout the vertebrata, with the resulting great diversity in environment, food, and conditions of life generally, was suggestive of the omnipresence of a specific malevolent agent of great vitality; that, with regard to the fluvial and marine fishes found bearing cancerous growths, this fact might well suggest that the specific cause of cancer is water-borne and, like the bacillus typhosus, it is not injuriously affected by sea-water; and, finally, that since the neoplasms found in fish are identical in every way with those occurring in man, infection may well have arisen through the agency of parasite-bearing sewage polluting both the rivers and the ocean into which they flow.

Regarding the third discovery of the transmissibility of cancer from one individual to another of the same

species, although this has had to be admitted, it is qualified by the assertion that such transmission is merely a transplantation of a graft of a malignant tumour and not the genuine inoculation of a specific disease. It would be more graceful to concede that since transmission between individuals of the same species is proved to be possible it may be eventually found that transmission between animals of different species, and even the development of one variety of malignant growth from another, is possible also.

An admission which may be looked for sooner or later is that a carcinoma of epithelial origin has been observed to give rise to a sarcoma in the adjacent connective tissue. Then will be confirmed the dictum that cancer is a specific infective disease and that one specific micro-organism is capable of originating every variety of malignant neoplasm, the variety depending upon, and only limited by, the anatomical diversity of the structure and the situation of the tissue invaded.

DEDUCTIVE EVIDENCE.

As it is necessary to apply the strictest canons of logic to the arguments brought forward in support of any hypothesis, I beg to submit the following, which to my mind fulfils this postulate. Every specific disease is infectious to the individual. By this term, "infectious to the individual," I mean the gradual evolution of disease, more or less rapid, locally and constitutionally, over the body from the point of origin of the disease. Specific diseases infectious to the individual are very numerous and are caused by the agency of some extrinsic parasite, either a microphyte or a microzoön. These diseases are communicated to others,

directly from individual to individual, or indirectly by inanimate objects, or through an intermediate host.

Now cancer is, emphatically, a specific disease, and it is intensely infectious to the individual; therefore, the only logical conclusion that can be drawn is that cancer is both transmissible to others and that it is caused by an extrinsic agent. Except for the solitary fact that the elements of a malignant neoplasm—i.e., its cells—are themselves transported, in addition to the infective agent (which is the peculiar and characteristic idiosyncrasy of cancer), this disease very closely resembles in its origin and evolution a chronic infectious disease.

My argument may be condensed into two syllogisms—viz. : 1.—All diseases which are infectious to the individual are transmissible to others. Cancer is infectious to the individual. Therefore cancer is transmissible to others. 2.—All diseases which are infectious to the individual have an external origin. Cancer is infectious to the individual. Therefore cancer has an external origin.

THE SPECIFICITY OF CANCER AND THE GENERAL PRINCIPLES OF ITS TREATMENT AND PROPHYLAXIS.¹

The treatment of disease is at all times beset with difficulty even when the cause is well known, and this difficulty is greatly enhanced in the case of maladies whose cause is still undetermined. In the latter class treatment can be only empiric. The cause of cancer has not, so far, been proved to demonstration, and unfortunately no remedy of any kind, even empiric, has been discovered; but though the cause has not yet been demonstrated by the production of the originating agent (and such is not remarkable since we are merely on the threshold of the knowledge of the causation of specific disease), still it is logically deducible from the well-known facts relating to the disease.

No disease more plainly bears upon itself the impress of specificity than cancer; indeed, this is one of its chief characteristics. Its constant primary local origin in practically any situation; its invariable extension by auto-infection, evidenced by its widespread dissemination by metastasis; its constant relation to a "condition precedent";² the innumerable so-called "coinci-

¹ An address delivered at a meeting of the East Yorks Division of the British Medical Association at Hull on March 18, 1910.

² The "condition precedent" is a term introduced to indicate that state of vulnerability which must exist before an individual can be successfully attacked by the cancer parasite. It is induced by degeneration of tissue from any cause, more especially from obsolescence of organs, senescence and senility, chronic disease, continued irritation, traumatism, and by congenital susceptibility.—A.T.B.

dences" which clearly point to what would, in any other diseased condition, be considered infection; and the countless successful inoculations which have been made, all testify to its true specific nature—i.e., to its being as typically infective a process as syphilis or tuberculosis.

Although analogy is quite incapable of proving anything, being merely a "resemblance in relations," yet even analogy is not wanting, for cancer is strikingly analogous to such parasitic diseases as syphilis, tuberculosis, and pyæmia, in spite of the fact that it possesses one peculiar idiosyncrasy of its own, inasmuch as its metastases are formed by proliferation of the transported cells of the primary focus. In all other similar diseases the infective agent is transported free, while in cancer it is conveyed encapsuled in a tissue cell. This is only another example of the extraordinary variety of parasites and their ways.

Strange to say, some non-believers in its exogenesis openly assert that cancer is a parasitic disease, but they allege that it is the cancer cell itself which is the parasite. They do not appear to be able to appreciate the obvious logical *sequitur* that, since no somatic cell can, *per se*, be a pathogenic parasite, there must of necessity be an intracellular influence which endues it with its malign parasitic power. In other words, there must be an intracellular parasite, and all parasites are extrinsic.

Why the extrinsic origin of cancer is not universally accepted is to me incomprehensible in the face of evident facts; but the sooner it becomes generally received the sooner is the search for the causative agent likely to be crowned with success, and the stigma of its unsuccessful treatment to be removed from the practice of medicine.

The concentration of research, based upon the logical hypothesis of exogenesis, must be more likely to be successful than the misdirected efforts of those who spend time and cerebral energy, not to speak of the great waste of money, in endeavouring to prove that a specific disease can possibly have an intrinsic origin, efforts which amount simply to beating the air.

It is generally admitted that all specific diseases, *except cancer*, arise by exogenesis—i.e., by infection from without—and that there is a known or suspected infective agent or parasite in each case which, so far as our present knowledge goes, is a micro-organism, either a microphyte or a protozoön, and that these diseases are communicated directly from individual to individual, or indirectly by inanimate objects, or through an intermediate host. With regard to cancer, I am convinced of its origin also by exogenesis, and that the infective agent resides in the invaded cells, although it has hitherto escaped detection.

I do not propose here to discuss the interesting problem why the hypothetical intracellular parasite of cancer has not been discovered, but I would remind you that the *Treponema pallidum*, responsible for syphilis, has only very recently been isolated, and that the parasite of small-pox and its bovine modification vaccinia (as well as that of many other specific diseases) still remains *perdu*.

That the infective agent of cancer resides in the invaded cell appears to me to be indisputable, since a single cell from a cancerous tumour is capable of reproducing the disease in another host, as has been proved by very many successful experiments, and an infected cell in the same host is capable of establishing a fresh

focus of disease in another situation, as is evidenced by the formation of metastases, and by the reappearance of the disease in, or near, a surgical cicatrix from cells left behind, or introduced into the wound by the surgeon's knife, which has set them free from the originating growth.

Further evidence of the existence of an intracellular malignant agent, or parasite, is derived from the fact that the parenchyma cells of a carcinoma have been observed by Ehrlich and Apolant to impart a malignant stimulus to the surrounding connective tissue cells, so giving rise to a true sarcoma. From this evidence it may also be deduced that one and the same species of parasite is sufficient to originate any and every variety of malignant neoplasm, such variety being determined by the nature of the tissue attacked, and limited only by the anatomical diversity of the tissues themselves. Hence the urgent necessity which exists for the detection of the elusive pathogenic principle, both in the invaded cells and in the lymph and blood.

The exact date of attack in cancer cannot be determined, for, unfortunately, there is no known initial or prodromal symptomatology, and the interval between invasion and extension by auto-infective dissemination is consequently unknown, but it is believed to vary with the situation and tissue of the primary focus and that it may be very short. It is obvious that if the date of infection could be known at the time, and if the site were accessible, immediate excision or other destruction of the invaded part would be the ideal method of treatment, for such might be confidently expected to be absolutely successful, just as syphilis can be successfully averted by the immediate destruction of its causative

parasite at the site of inoculation. Such data, however, with regard to cancer, in our present state of knowledge, are available only in the case of experimental or deliberate inoculation.

The bar to success in treatment is that it is never called for until the disease has given unequivocal evidence of its existence as a distinct tumour, and even where appearances might suggest an early and purely local invasion, widely disseminated extension, hopelessly beyond the surgeon's reach, has in all probability already occurred. It should, therefore, be a surgical axiom that if any inaccessible foci—e.g., infected lymphatic glands—are known or suspected to exist, as metastases of an accessible primary neoplasm, operation with a view to the removal of the latter is not only inadvisable but unjustifiable, for such a procedure would be utterly futile for the eradication of the disease. Not only, indeed, would operation in such circumstances be futile and unscientific, but it would probably be the actual cause of increase in the activity of the malignant process, by setting free, and scattering broadcast, infected cells hitherto confined, so that the last state of the patient would be worse than the first, and even life itself would be materially shortened. The presence of inaccessible foci does not, however, negative purely palliative operative procedures, such as the relief of oedema of the arm by lymphangioplasty, as devised by Sampson Handley, or the removal of necrosed and offensive tissues.

Unless distant extension is obvious free excision of the accessible diseased area, including infected lymphatic vessels and glands and adjacent structures—e.g., muscles, and especially fascia—may be attempted as *the*

first line of treatment (vis a fronte), the surgeon bearing in mind that every single infected cell left behind or set free by his knife is a potential agent in causing a local and general recrudescence of the disease.

Although very exceptional cases have been recorded where tumours, undoubtedly malignant, have disappeared spontaneously, and although surgical removal of such tumours has apparently cured the disease in some cases, it is more than doubtful if any operative treatment of accessible malignant neoplasms is ever successful in the complete eradication of cancer; for by the time that a tumour has been discovered far-reaching infection has almost certainly already taken place. But for the incidence of fatal intercurrent disease, the malignant process must have inevitably reasserted itself sooner or later and eventually claimed its victim.

It is a marked characteristic of cancer, and one which it shares with syphilis, that it may remain quiescent for a time. Thus, a distant metastatic focus may remain dormant for an indefinite period, the victim being lulled into a false sense of security, to light up at last into fatal activity, while the final site of the disease may be so remote from the original focus as to mislead the surgeon as to its true nature.

As a concrete example of this I may quote a case of Sir Hector Cameron's. In 1894 he removed the left mamma from the patient of a medical friend. In 1903 this patient began to complain of so-called "rheumatic" pain in her left hip and thigh, which became so severe as to cause her to go to bed and have medical attendance. One day, on getting out of bed, the left femur spontaneously fractured. Her medical attendant could find no trace of cancer in any other part of her

body, but the patient died from gradual exhaustion without any evidence of farther dissemination in lungs, liver, or bone. Here some infective particle, lymph conveyed, had metastatically resided in the medulla of the femur for nine years, making no sign, until at last waking into activity by quick growth gave rise to pressure, pain, destruction of bone, spontaneous fracture, and death from exhaustion. There can be no reasonable doubt but that if this patient had died during the interval from intercurrent disease—e.g., pneumonia—she would have been declared cured by operation of her original cancerous disease. Many other instances might be adduced where recurrence, subsequent to operation on the breast for malignant disease, has occurred in other situations—e.g., the vertebræ, brain, &c.—and after even longer periods of quiescence, but that just quoted will serve as an example.

This period of dormancy suggests that all infected cells are not equally active—i.e., that the hypothetical intracellular parasite is not always in the same state of development, some cells containing it in an intermediate form, which form remains quiescent until some unknown stimulus or time and circumstances favour its further evolution. Such a hypothesis would explain many otherwise inexplicable clinical facts relative to cancer.

It is evident, therefore, that want of success after surgical treatment must be attributed either to incomplete removal or to the occurrence of distant dissemination prior to operation.

Unsatisfactory as surgical treatment is in cases of accessible primary disease, there can be no hope from the surgeon where the neoplasm is inaccessible from the

first or where it has shown itself to have become so after operation. Dark indeed must the prospect appear to the man who believes cancer to be a constitutional disease with local manifestations and having an intrinsic origin, for even the surgeon can do nothing for its removal. After all, the surgeon can only be expected to deal with what he can see, and temporarily stave off impending death threatened by mechanical causes; he cannot reach the cause. Cancer is practically ineradicable by surgical means alone, for the reason already stated. If cancer is ever to be successfully treated, the cause itself must be attacked, and this can be done only by specific means. This constitutes *the second line of treatment (vis a tergo)*.

The surgeon confronted with a fully developed Hunterian ulcer is powerless to avert constitutional dissemination by the knife—indeed, it has already occurred. In like manner he cannot expect to eradicate cancer which has already become constitutional by local excision of its visible manifestation. The physician, on the other hand, in the case of syphilis, can view the local indication of the disease with equanimity, for he knows that he is able to combat constitutional disease successfully by proved specific remedies.

Cancer being as truly specific a disease as syphilis, and since the latter yields to internal specific treatment, it is reasonable to assume that the former will likewise be amenable to the same. In such treatment appears to lie the only hope of the victim of cancer, and well will it be for him when it has been established that this disease is due to an extrinsic cause, for recovery may then be hopefully looked for from appropriate remedies. Should the infective agent prove to be a protozoön, as is the

case in syphilis, malaria, &c., and my belief is that the probability is in favour of such a parasite, then a parasiticide is indicated, similar in lethal action to those found effectual in these diseases. Among the methods of exhibiting such parasiticide kataphoresis of accessible neoplasms would doubtless commend itself.

The parasiticide specific for cancer must be sought for by experiment both on man and the lower animals; and I should imagine that investigators would find no more willing, nay zealous, co-operators than the human subjects of cancer themselves.

On the other hand, should the causal agent be found to be a bacterium, success may follow the exhibition of a cancer vaccine, prepared after the methods of Wright; or of an anti-cancerous serum. Until such serum can be procured from an individual cured of, or rendered immune to, the disease, the effect of auto-serum might be tried. This may contain a self-generated antitoxin; or, if it contains the toxin itself, its injection in small amount may act as a vaccine and stimulate the leucocytes to increased phagocytic activity.

In September, 1907, a man, aged 67, was admitted to the Driffeld Poor Law Infirmary suffering from disease of the left elbow. He said he had been discharged from a city infirmary in the neighbourhood as incurable, having refused offered amputation. His elbow presented the appearance of a huge fungating epithelioma, a mass covered with suppurating granulations, discharging freely and emitting a most vile odour. There was great pain present which prevented sleep.

I decided to experiment on this man by injecting auto-serum and explained to him what would have to be

done, expressing the hope of relief if not of cure. He was as eager as myself to try this treatment, and gladly consented.

Ten c.cm. of blood were drawn from the right median basilic vein by a large antitoxin syringe and allowed to coagulate in a sterilized test tube. The serum was then poured off, centrifuged, and stored in 0.5 c.cm. ampoules and sealed up. The ampoules were then sterilized. On September 25th, 1907, 0.5 c.cm. was injected hypodermically into the posterior aspect of the right forearm, and a similar dose was given weekly until the supply was exhausted. Fresh supplies of blood were drawn as required and treated as before, and the injections were continued until twenty-three had been given, the last being given on February 23rd, 1908. After several injections there was marked improvement. Pain disappeared entirely and rapid diminution of the mass set in, the discharge gradually ceased, and by the time that the last injection was given only a few small granulations remained, the elbow being normal in size.

Though greatly elated by the success of this treatment I felt it desirable to make certain of the nature of the disease. A few granulations were detached and sent to the Clinical Research Society. To my great chagrin the report stated that the disease was tuberculous.

As my thoughts and efforts were concentrated upon the treatment of cancer, I was too greatly disappointed to care to report the successful result of the action of auto-serum in tuberculous disease, and it may be that further experiment by others will confirm my experience and that another weapon may be provided against a disease which is quite as malignant as cancer, or disprove it.

In several cases of undoubted cancer, in private practice, I attempted the same treatment, but in every case the patient refused to permit me to obtain a second supply of blood, and I was thus prevented from bringing my experiments to a positive or negative conclusion.

The fact that one was only a general practitioner was too heavy a handicap, but, in hospitals for cancer, with proper laboratory facilities, this method of treatment might be thoroughly tested, since at least some of the patients might be found to be as willing, in their own interests, to co-operate with the surgeon as my patient was. At the same time success is, in my opinion, only probable on the presumption that the parasite responsible for cancer is a microphyte and not a protozoön. In the latter case some mineral parasiticide is indicated such as is successful in syphilis. Molybdenum has not been tried, and if a collosol of this metal can be prepared I should be glad to experiment with it, and there is abundant material.

From the foregoing considerations I would submit that the successful treatment of cancer will consist in the removal by surgical means of accessible tumours, more especially those threatening life from mechanical causes, combined with the internal administration of specific remedies, the latter being relied upon to check the further spread of disease and neutralize that already existing, by destroying the causal parasite; while inoperable disease, whether accessible or inaccessible from the first, can only be treated by specific remedies and such non-operative mechanical means as fulguration, X rays, radium emanations, kataphoresis, &c.

The late Dr. Forbes Ross, in his book, "Cancer, the Problem of its Genesis and Treatment," published in

1912, states his belief that cancer is due "to a want of balance in particular mineral salts in the body," and his belief that "the disturbance of the potassium balance in the body is the cause, or one of the main causes, of epithelial cancer."

On this belief Dr. Ross based his treatment of cancer by large doses of potassium salts, and claimed success both in its cure and prophylaxis.

With regard to the latter he states that he always prescribed potassium salts where other doctors prescribed those of sodium. He laid emphasis on the fact that "not in one single instance have any of the numerous patients that I have habitually cared for, during fifteen years, developed in any part of their body whatsoever a single cancer amongst them all. *Actually not one single case of cancer has ever to my knowledge occurred amongst the clientele of my practice.*"

While I have no hesitation in asserting that Dr. Ross was quite mistaken in believing that such a specific disease as cancer could be due to a want of balance, in the body, of potassium salts, I freely admit that this want of balance may possibly greatly contribute to the production of the "condition precedent." Potassium in full amount, or even in excess, may very well be inimical to the cancer parasite, discouraging its growth and extension by producing an uncongenial soil, and even prove destructive to its existence. Its microbicidal property would be enhanced by its innocuousness, which is wanting in other microbicides such as mercury and arsenic.

Potassium may be used freely without risk, for its supposed malign action on the heart is, in my opinion, very greatly exaggerated. Even if, in some cases, the

heart may appear to be affected, it may be easily protected, as is pointed out by Dr. Ross, by the simultaneous administration of strophanthus and strychnine.

Let it be thoroughly tried. *Experientia docet.*

No less important, or even more important, than the curative treatment of cancer is its prophylaxis. It is a truism that "prevention is better than cure," although this naturally is not the dominant sentiment of the sufferer from the disease.

Everything that tends to the encouragement of the "condition precedent" should be avoided. We cannot, indeed, stay the flight of time, that *edax rerum* which brings in its wake senescence, senility, and the obsolescence of organs, which play so important a part in the incidence of cancer, but these may be greatly mitigated by a strict observance of all the well-known laws of health.

Cremation of the cancerous cadaver is imperative, since such would remove a very obvious risk of perpetuation of the cause of the disease when earth burial is resorted to—e.g., by the action of earthworms, which convey soil from a depth of 6 to 8 feet to the surface, and by the contamination, by percolation, of the sources of water-supply. All dressings of cancerous wounds, all discharges and dejecta from cancerous patients should be destroyed, preferably by fire. There should be thorough disinfection of all rooms and houses inhabited by those suffering from, or who have died from, cancer. Intimate personal contact with the diseased should be avoided as far as possible. Personal cleanliness should be scrupulously observed, especially in the washing of the hands before eating, and in the

preparation of food. There should be perfect sterilization of all water and food partaken of, especially when the latter is eaten in an uncooked condition; and the contamination of any food by the lower animals, or by flies, should be prevented.

If there is any truth in the allegation that the earth-worm is an intermediate host, and that the soil is one habitat (water being another) of the parasite, the mere idea of eating raw vegetables, however well scrubbed and apparently clean, becomes repulsive, and is calculated to induce one to ponder over the desirability or otherwise of total abstinence from all uncooked fruits and vegetables which lie on or in the surface of the ground.

Finally, notification of all cases of cancer should be enforced.

Sir J. Bland-Sutton, in his recent work, "Cancer Clinically Considered," says:—

"The frequency with which cancer attacks the large intestine is in favour of those who believe that cancer is due to a micro-parasite, probably something which is taken in with uncooked food or with water. Indeed, I feel so strongly on this matter that for many years I have avoided eating all sorts of uncooked vegetables. Much as I enjoy salad with my chicken, or my cheese, I do not touch it. However clean your celery may appear to be, if you pull aside the stalks immediately round the centre, which is about the only part worth eating, you will see that there remains some dirt which has not been washed away. One feels deeply thankful that most of the food eaten by mankind is cooked. Partially cooked or "underdone" meat carries penalties in the way of entozoa, and Metchnikoff says that

“entozoa may serve as gates of entry for the hypothetical parasites of carcinoma.” Food and water are essential to life, and it is undeniable that they are the frequent purveyors of disease, and that minute animal parasites are our daily messmates and table companions, though their presence is sublimely ignored by us. In Behla’s opinion the probable vehicle of infection in cases of cancer occurring in Luckau in Germany was the uncooked vegetables.”

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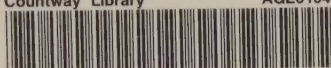
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